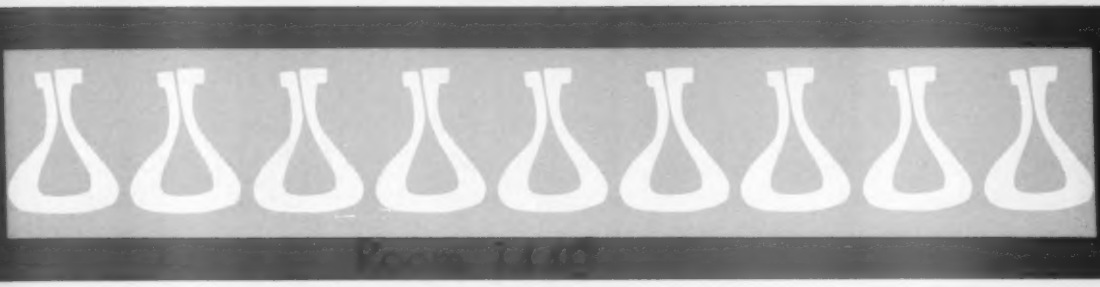

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PSYCHOPHARMACOLOGY ABSTRACTS

NATIONAL INSTITUTE OF MENTAL HEALTH

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ABSTRACTS

PRECLINICAL PSYCHOPHARMACOLOGY

01 CHEMICAL SYNTHESIS, ISOLATION AND CHARACTERIZATION

080337 Gewirtz, George P.; Kopin, Irwin J. Laboratory of Clinical Sciences, National Institute of Mental Health, Building 10, Room 2D-46, Bethesda, Maryland 20014 Effect of intermittent nerve stimulation on norepinephrine synthesis and mobilization in the perfused cat spleen. *Journal of Pharmacology and Experimental Therapeutics.* 175(2):514-520, 1970.

The effect of intermittent nerve stimulation on norepinephrine synthesis and mobilization in the perfused cat spleen is studied. It was found that norepinephrine-C14 is synthesized in the spleen perfused with tyrosine-C14 and is released during nerve stimulation. There is a more rapid increase in the specific activity of released norepinephrine-C14 from spleens stimulated every 2 minutes than in that released from spleens stimulated every 10 minutes. After 3000 impulses delivered at 30 impulses/sec at intervals of either 2 minutes or 10 minutes, the specific activity of the released norepinephrine-C14 is greater than that remaining in the spleen, indicating selective release of newly synthesized norepinephrine. The ratio of the specific activity of norepinephrine-C14 released to that remaining in the spleen is higher than more frequent stimulation. In the presence of phenoxybenzamine the rate of increase of the specific activity of released norepinephrine-C14 is more rapid than in its absence; there is selective release of newly synthesized norepinephrine, but the ratio of specific activity of released to splenic norepinephrine-C14 is lower, indicating more rapid equilibration of norepinephrine stores as well as more rapid synthesis of the catecholamine. After perfusion for 4 hours the specific activity of the released norepinephrine-C14 is about 0.7of the specific activity of norepinephrine totally derived from the perfused tyrosine-C14. These results suggest that newly synthesized norepinephrine plays a significant role in maintaining transmitter release and that this role varies with the interval between stimulation. 18 references. (Author abstract modified)

080338 Gumulka, W.; Samanin, R.; Valzelli, L. Department of Experimental Pharmacology, Academy of Medicine, Warsaw, Poland Effect of chlorpromazine on 5-hydroxytryptamine metabolism in hippocampal stimulated rats. *European Journal of Pharmacology (Amsterdam).* 12(3):276-279, 1970.

The effect of chlorpromazine on 5-hydroxytryptamine metabolism in hippocampal stimulated rats is reported. It was shown in this study that electrical stimulation of the dorsal hippocampus in rats induces behavioral effects as well as an increase of 5-hydroxyindolacetic acid content in both anterior and posterior parts of the brain, without significantly affecting the level of 5-hydroxytryptamine. Chlorpromazine, 1mg/kg intraperitoneally (i.p.), blocks the behavioral effects but the biochemical effects are only inhibited by 10mg/kg i.p. 18 references. (Author abstract modified)

02 DRUG DEVELOPMENT (PRECLINICAL SCREENING)

075957 McClearn, Gerald E.; Nichols, David. Institute for Behavioral Genetics, University of Colorado, Boulder, Colorado 80302 Effects of intraperitoneal injection of ethanol on ethanol ingestion of C57BL mice. *Psychonomic Science.* 20(1):55-56, 1970.

When intraperitoneal injections of an ethanol solution are given to C57BL mice (an alcohol preferring strain), their free choice ingestion of ethanol during the next 24 h is reduced by an amount approximating the injected amount. The ethanol intake control system of these mice is evidently not dependent upon taste or other stimuli associated with ingestion. 3 references. (Author abstract)

076576 Hudson, R. D.; Wolpert, M. K. Brown University, Providence, Rhode Island Anticonvulsant and motor depressant effects of Diazepam. *Archives Internationales de Pharmacodynamie et de Therapie (Belgium).* 186(2):388-401, 1970.

Anticonvulsant and motor depressant effects of Diazepam were investigated using mice, cats and dogs. Doses of Diazepam (0.4-10 mg/kg, i.p.)were demonstrated to significantly protect mice from the convulsive and lethal effects of Pentetrazole and electroshock. Diazepam (5-10 mg/kg, i.v.)induced sleep in cats with chronically implanted electrodes but no characteristic electroencephalographic changes were noted. Spinal motor reflexes and evoked potentials recorded from

spinal roots (L7-S1) were significantly depressed in response to doses of Diazepam while the neuromuscular preparation was unaffected. 18 references. (Author abstract)

079988 Hoffmann, Irmgard; Kuch, H.; Schmitt, K.; Seidl, G. Farbwerke Hoechst AG, vorm. Miester Lucius u. Bruning, 6230 Frankfurt 80, Germany /2-Ethylamino-6-chloro-4-methyl-4-phenyl-4H-3,1-benzoxazine, , a new psychotropic compound./ 2-Athylamino-6-chlor-4-methyl-4-phenyl-4H-3,1-benzoxazin, eine neue, psychotrope Verbindung. *Arzneimittel-Forschung (Aulendorf).* 20(7):975, 1970.

The synthesis and pharmacological properties of the new psychotropic compound 2-ethylamino-6-chloro-4-methyl-4-phenyl-4H-3, 1-benzoxazine (Hoe 36 801) are reported. According to the action on animal behavior, Hoe 36 801 may be considered a tranquilizing drug with additional stimulating properties. 2 references. (author abstract

080032 Loev, Bernard; Goodman, M. M.; Zirkle, C.; Macko, E. Smith, Kline & French Laboratories, 1530 Spring Garden Street, Philadelphia, Pennsylvania 19101 A benzazepinone: carbon analog of diazepam. *Arzneimittel-Forschung (Aulendorf).* 20(7):974-975, 1970.

The carbon analog of 2H-1,4-benzodiazepin-2-one (diazepam) wherein the imino nitrogen has been replaced by a methine giving a 1-benzazepin-2-one, has been prepared and found to possess little if any of the central nervous system depressant effects of diazepam, when administered to rats at a dose of 200mg/kg, orally. The only observed effect was a slight irritability and a weak inhibition of metrazol induced seizures. The compound also had no significant effect on blood pressure of rats or dogs. 2 references. (author abstract modified)

03 MECHANISM OF ACTION: PHYSIOLOGICAL, BIOCHEMICAL AND PHARMACOLOGICAL

075845 Sethy, Vimala H.; Pradhan, Ratan J.; Mandrekar, S. S.; Sheth, U. K. Department of Pharmacology, Seth G. S. Medical College, Parel, Bombay-12, India Role of brain amines in the analgesic action of meperidine hydrochloride. *Psychopharmacologia (Berlin).* 17:320-326, 1970.

The role of brain amines, catecholamines and indoleamines, on the analgesic action of meperidine hydrochloride was investigated by various methods in pretreated mice. The effect of reserpine, alpha-methyl-dl-m-tyrosine (alpha-MT) and p-chlorophenylalanine (p-C1'ell'Phe) pretreatment on meperidine analgesia has beenstudied by the tail clip, hot plate and electric shock methods in male mice. The effective dose, median (ED50) of meperidine was significantly increased by all methods when the animals were pretreated with reserpine. Alpha-MT significantly increasedthe ED50 of meperidine only by the clip method. p-C1'ell'Phe pretreatment significantly increased the ED50 of meperidine by the clip (both in acute and chronic treatments) and shock methods (only after chronic treatment). Possible explanations for the different findings are discussed. The exact role of biogenic amines in meperidine induced analgesia remains uncertain. 23 references. (Author abstract modified)

075846 Contreras, E.; Tamayo, L.; Weitzman, P. Department of Pharmacology, University of Concepcion, Concepcion, Chile Reduction of the antinociceptive effect of 5-hydroxytryptophan in morphine tolerant rats. *Psychopharmacologia (Berlin).* 17:314-319, 1970.

To obtain further information on the effect of 5-hydroxytryptophan on the analgesic response in rats tolerant to morphine, the experiments reported here were performed. The effect of 5-hydroxytryptophan on pain threshold was studied in rats both tolerant and nontolerant to the analgesic action of morphine as assessed using a procedure of electrical stimulation. The compound elevated pain threshold and exhibited an additive effect with morphine analgesia in nontolerant rats. A marked reduction of the antinociceptive action of the serotonin precursor as well as absence of the additive effect with morphine was observed in rats tolerant to the analgesic. These results are discussed in terms of the possible mechanism of action of serotonin on morphine effects. 17 references. (Author abstract modified)

075851 Morse, David L.; Solomon, Paul R. State University College, New Paltz, New York 12561 The effects of tricyanoaminopropene on learning in a differential reinforcement of low rates situation. *Psychonomic Science.* 20(1):3-4, 1970.

To determine if the effects of tricyanoaminopropene (TRIAP) are to actually enhance learning or merely to act as a stimulant and therefore facilitate performance, rats were

used in experiments employing differential reinforcement of low rates (DRL) situation. Thirty male Wistar rats were assigned randomly to 1 of 6 groups (6, 12, or 24mg/kg of TRIAP, .2or .8mg/kg of d-amphetamine, or a control group receiving .3% tragacanth). All subjects were trained on a DRL 5 and DRL 10 sec schedule of reinforcement. With the DRL 10 sec schedule it was found that the animals injected with TRIAP reached the criterion for learning in significantly fewer trials than did the d-amphetamine and control groups. This suggests that the beneficial effects of TRIAP are due to a learning rather than a stimulant effect. 4 references. (Author abstract modified)

076068 Spigel, Irwin M.; Ramsay, Alex. Department of Psychology, University of Toronto, Toronto 181, Ontario, Canada Extinction of the excretory alkali metal response (EAMR) to stress in a reptile. ***Psychonomic Science.*** **19(5):261-263, 1970.**

Some parameters in the extinction of the stress induced potentiation of sodium and potassium excretion in turtles were examined in 3 experiments. A pattern similar to that of a conditioned response decrement was obtained with termination of shock, and the sensitivity of excretory alkali metal response extinction to differential antecedent shock administration was demonstrated. It was also found that the increment in cation excretion, following shock administration in a consistent daily pattern, was much more resistant to extinction than that observed in randomly shocked subjects. The difficulty in reconciling these results with those from other species and using other procedures is discussed. 5 references. (Author abstract)

076132 Houser, Vincent P. University of Massachusetts, Amherst, Massachusetts 01002 The effects of adrenergic and cholinergic agents upon eating and drinking in deprived rats. ***Psychonomic Science.*** **20(3):153-155, 1970.**

The effects of cholinergic and adrenergic agents on feeding and drinking behavior in deprived rats was investigated. Both scopolamine hydrobromide and scopolamine methylbromide reduced food intake, while decrements in water comsumption were caused only by scopolamine hydrobromide. Dextroamphetamine sulfate reduced food intake but did not affect water consumption. Finally, both pilocarpine nitrate and DL-alpha-methyl-p-tyrosine had no effects on either measure. These results confirm Stein's suggestion that anticholinergic agents decrease eating via their peripheral effects while blocking drinking through their central activity. It was suggested that the motivational effects of these agents should be considered whenever these drugs are administered to animals that are under the control of appetitively motivated schedules of reinforcement. 14 references. (Author abstract)

076186 Lal, Harbans; Puri, Surendra K.; Fuller, George C. Department of Pharmacology, University of Rhode Island, Kingston, Rhode Island 02881 Inhibition of hepatic hexobarbital metabolism by dextro amphetamine. ***Psychopharmacologia (Berlin).*** **16(5):395-398, 1970.**

In mice, d-amphetamine injected intraperitoneally (10mg/kg, 1 hr before sacrifice) decreased in vitro hepatic metabolism of hexobarbital. Since the addition of d-amphetamine to liver homogenates in vitro also inhibited the hexobarbital metabolism, the in vitro effect of amphetamine was not due to its pharmacodynamic action. Implications for drug interactions between amphetamines and some central nervous system depressants in human psychopharmacology are noted. 8 references. (Author abstract modified)

076239 Wade, George N.; Zucker, Irving. Department of Psychology, University of California, Berkeley, California 94720 Development of hormonal control over food intake and body weight in female rats. ***Journal of Comparative and Physiological Psychology.*** **70(2):213-220, 1970.**

Information is provided on developmental aspects of hormonal control over alimentary regulation and changes in body weight of rats ovariectomized on the day of birth or at weaning. Ovariectomy has no effect on body weight until after puberty when spayed females weigh significantly more than intact controls. Treatment with estradiol benzoate (EB) does not decrease food intake or body weight until rats are approximately 40 days old. Onset of responsiveness to estrogens is, however, independent of puberty. Hypophysectomy greatly increases responsiveness to EB among prepubertal females. It is suggested that prepubertal pituitary secretions eliminate ventromedial hypothalamic (VMH) restraint over food intake; since estrogens act on the VMH to depress eating, this may account for the lack of effect of EB on food consumption in immature rats. Amphetamine injections depress food con-

sumption during prepubertal periods when estrogens are ineffective; it is suggested that amphetamine acts directly on the lateral hypothalamus which is not refractory during the prepubertal period. 30 references. (Author abstract modified)

076554 Zumpe, D.; Michael, Richard P. Primate Behavior Research Laboratories, Institute of Psychiatry, Bethlem Royal Hospital, Monks Orchard Road, Beckenham, Kent, England Ovarian hormones and female sexual invitations in captive rhesus monkeys (Macaca mulatta). *Animal Behaviour (London).* 18(2):293-301, 1970.

Observations were made on female sexual invitations occurring during 60 min tests with 12 oppositely sexed pairs of adult rhesus monkeys when ovariectomized females were treated with oestradiol and progesterone (588 tests). Like presentations, hand reaches and head ducks increased when females received oestradiol and became receptive, and decreased when they received progesterone in addition and became unreceptive. In 3 pairs progesterone appeared to exert a biphasic action; stimulation at lower doses changing to suppression as doses were increased. When females received progesterone alone, refusals increased and invitations decreased; hand reaches, head ducks and head bobs being abolished. The 3 latter invitations were positively correlated with each other but not, however, with presentations, suggesting that hand reaches, head ducks and head bobs might have a common derivation. The view was presented that these 3 gestures are ritualized components of threat behavior serving exclusively a sexual initiating function, and that total invitations are a more useful index of female receptivity than presentations alone. 16 references. (Author abstract)

078378 Glassman, E.; Henderson, A.; Cordle, M.; Moon, H. M.; Wilson, J. E. Department of Biochemistry, University of North Carolina, Chapel Hill, North Carolina 27541 Brain function and macromolecules: V. the effect of cycloheximide and actinomycin-D on learning in the headless cockroach. Progress Report, NIMH Grant MH-15897, 1970. 8 p.

It is confirmed that cycloheximide can produce a decrement in learning performance in the headless cockroach. Actinomycin-D has similar effects. Although one cannot rule out the necessity of macromolecular synthesis for the learning process in this preparation, the increase in leg activity caused by these drugs makes it likely that their effects on learning performance are due to an interference with the quiescent state required to keep the leg raised. This highly likely alternative casts doubt on the interpretation that RNA and protein synthesis is involved in primary acquisition in this preparation. 8 references. (Author abstract)

079179 Billiet, M.; Bernard, P.; Delaunois, A.; De Schaepdryver, A. Catedra de Farmacologia Experimental, Facultad de Farmacia y Bioquimica, Buenos Aires, Argentina Induced changes in caudate nucleus dopamine and electroshock threshold. *Archives Internationales de Pharmacodynamie et de Therapie (Belgium).* 188(2):396-400, 1970.

An attempt is made to correlate the levels of caudate nucleus dopamine and whole brain noradrenaline and the electroshock threshold in rabbits by inducing changes in the dopamine level and in electroshock threshold. Reserpine, pargyline, L-dopa, diethyldithiocarbamate, prenylamine and some combinations of these compounds were administered to the rabbits. It was found that electroshock threshold may be modified by changes in brain amine levels. Increased levels of caudate nucleus dopamine enhance electroshock threshold. However, decrease of electroshock threshold is not exclusively correlated with levels of caudate nucleus dopamine, but also with whole brain noradrenaline levels. 10 references. (Author abstract modified)

079355 no author. author address not given Rx for agitated depression. *Medical World News* 12(6):32B, 1970.

A new regimen for treatment of agitated depression and associated hypoglycemia is reviewed and evaluated. The rationale for the regimen, consisting of imipramine, atropine, diet and thyroxine, is that the depression is mediated in trophotropic centers of the hypothalamus, areas whose ascending circuits can synchronize high amplitude, slow wave cortical electroencephalographic activity, as sleep does, while the descending circuits stimulate parasympathetic activity. At the same time the depression occurs, the trophotropic centers stimulate the vagus nerve, incuding hyperinsulinism which leads immediately into hypoglycemia. The treatment, reasons for the elements, clinical trials, and a possible flaw in the theory are discussed.

079951 Holm E.; Boettger, F.; Konig, J. W.; Reith, H.-J. Medizinische Klinik im Klinikum Mannheim der Universitat Heidelberg, Theodor-Kutzer-Ufer, 68 Mannheim, Germany /Effects of chlorimipramine on electrical activities of subcortical brain structures and of sympathetic nerves./ Einflusse von chlorimipramin auf elektrische aktivitaten subcorticaler hirngebiete und sympathischer nerven. *Arzneimittel-Forschung (Aulendorf).* 20(7):896-901, 1970.

Acute experiments with intravenous injection of chlorimipramine were carried out in 25 cats. In 19 animals (encephale isole) evoked potentials were elicited by central stimulation (single shocks: 0.2msec; paired shocks: 0.2msec, intervals 20 to 200 msec) and recorded with bipolar electrodes from subcortical regions of the brain. An electronic averager was used for threshold evaluation of single shock responses and for measurements of excitability cycles. Chlorimipramine (0.5to 3.0mg/kg) significantly lowered the thresholds of several efferent projections of the amygdaloid nucleus. In contrast, the caudate nucleus and the pontine reticular formation exhibited an increase in the thresholds of their efferent projections following administration of 1.0mg/kg. The excitability cycles of 2 intralimbic connections (amygdala - hippocampus; hippocampus - amygdala) revealed inhibitory effects of the substance (0.5to 8.0mg/kg). With 0.75mg/kg or less, electrocortical and hippocampal arousal patterns produced by reticular stimulation remained unaffected. In further experiments on intact cats, 2 anesthetized with pentobarbital and 4 unanesthetized, spontaneous potentials of renal sympathetic nerves were reduced by chlorimipramine (0.5to 3.0mg/kg), independently of blood pressure alterations. Certain clinical actions of the drug may be due to changes in the excitability of the amygdaloid nucleus and the sympathetic system. 55 references. (author abstract)

079954 Estler, C.-J.; Ammon, H. P. T. Pharmakologisches Institut der Universitat Erlangen-Nurnberg, Universitatstrasse 22, 852 Erlangen, Germany /Antagonistic influence of beta-sympathicolytics on the metamphetamine-induced changes in function and metabolism of the brain./ Antagonistischer Einfluss von beta-Sympathicolytica auf die durch Metamphetamin verursachten Anderungen von Funktion und Stoffwechsel des Gehirns. *Arzneimittel-Forschung (Aulendorf).* 20(7):908-909, 1970.

Metamphetamine (3 micrograms/g s.c.)produces excitation and enhanced motor activity in mice. It stimulates glycogenolysis and glycolytic carbohydrate breakdown in the brain. The beta-receptor blocking agents DL-propranolol (5 micrograms/g i.p.)and D-(--)-N-isopropyl-p-nitrophenylethanolamine (INPEA) (25 micrograms/g i.p.)depress metamphetamine produced motor excitation and, at the same time, inhibit the influence of metamphetamine on the carbohydrate metabolism of the brain. It is concluded that adrenergic mechanisms take part in the metamphetamine induced increase of CNS function and play an essential role in the effects of metamphetamine on cerebral carbohydrate metabolism. 14 references. (author abstract)

079961 Lorenz, Dietrich. Troponwerke Dinklage and Company, Berliner Strasse 220, 5 Cologne 80, Germany /Combination test on the analgesic effect of dextropropoxyphene and some psychotropic drugs in the mouse./ Kombinationsversuche uber die analgetische Wirkung von Dextropropoxyphen und einigen Psychopharmaka an der Maus. *Arzneimittel-Forschung (Aulendorf).* 20(7):925-928, 1970.

When combining flupentixol and clopenthixol with dextropropoxyphene it was found that the analgesic effect both in the benzoquinone test and in the hotplate test was enhanced more than additively (potentiation). In the hotplate test the enhancement was particularly pronounced with flupentixol. In a sedation test (balance) the enhancement of effect was not over additive, from which it can be concluded that the described combinations may well intensify the reflex inhibition found in the analgesic test but not the sedative effect. Meprotixol, amitriptyline, and nortriptyline showed either an over additive efficiency increase of combination in the benzoquinone test, or like chlorprothixen, increased the sedative activity, too. Chlorpromazine in combination with dextropropoxyphene showed a purely additive enhancement of analgesic and sedative effects. 6 references. (author abstract)

079968 Lewi, P. J.; Heykants, J. J. P.; Allewijn, F. T. N.; Dony, J. G. H.; Janssen, P. A. J. Research Laboratories, Janssen Pharmaceutica, Beerse, Belgium Distribution and metabolism of neuroleptic drugs: Part I: Pharmacokinetics of haloperidol. *Arzneimittel-Forschung (Aulendorf).* 20(7):943-948, 1970.

The pharmacokinetic properties of the potent neuroleptic drug 4-(-4-(p-chlorophenyl)-4-hydroxy-piperidino)-4'-fluorobutyrophenone (haloperidol, R 1625) were studied in brain, liver, blood, urine and feces of Wistar strain rats. Specifically tritium labelled haloperidol was injected s.c. at 8 dose levels and its activity was measured at 8 different times after administration. The experimental data were analysed by computer, using polynomial regression. The concentrations of unmetabolized drug in brain, liver and blood show abnormal dose dependence. Brain levels can exceed corresponding blood levels by a factor of 10. A qualitative model is proposed, based on saturable brain and liver compartments. The median effective doses obtained in amphetamine antagonism and apomorphine antagonism in rats correspond with the same overall amounts in the brain 70 and 270 nanograms. 13 references. (author abstract)

079972 Cocchi, Angelo; Andreola, M. L. Psychiatrische Klinik der Universitat Mailand, Via G. F. Besta 1, Milano-Affori, Italy /Morphological aspects of application of noxiptilin (BAY 1521) in animal experiments./ Morphologische Aspekte der Verabreichung von Noxiptilin (BAY 1521) im Tierexperiment. *Arzneimittel-Forschung (Aulendorf).* 20(7):958-963, 1970.

Experiments were conducted on mice on a new antidepressive drug, 5-(2-dimethylamino-ethoxy-imino)-5H-dibenzo(a,d)cyclohepta-1,4-diene hydrochloride (BAY 1521, Agedal). Three different doses (0.33, 0.02, and 0.005 LD50) were given. With the first 2 doses hypermotility, without hypotonia, was observed having an intensity and duration proportionate to the dosage. With the third dosage, a tranquilizing effect without evidence of muscular hypotonia was observed after an initial excitement. Pericellular and intracellular edema, and morphological alterations in the thalamic neurones were found with every dosage. By comparing the action of BAY 1521 with that of imipramine and amitriptyline, it is concluded that the new derivative may be related to amitriptyline because of its effects on the symptomatology, but differs from both drugs because of its mode of action on cellular morphology and its site of action. 20 references. (author abstract modified)

079997 Hudson, R. D.; Wolpert, Mary K. Section of Neuroscience, Division of Biological and Medical Sciences, Brown University, Providence, Rhode Island Central muscle relaxant effects of diazepam. *Neuropharmacology (Oxford).* 9(5):481-488, 1970.

Motor depressant effects of diazepam were studied in the intact, decerebrate and high spinal cat. Diazepam (0.125-16mg/kg, i.v.)produced a depression of both the patellar and linguomandibular reflexes in the intact cat. In the high spinal (C1) cat only the linguomandibular reflex was depressed. Facilitation and inhibition of the patellar reflex elicited in both intact and high spinal (Cl) cats were reduced by diazepam. No depression was observed in the in vivo neuromuscular preparation of the tibialis anticus muscle. Small doses of diazepam (0.125mg/kg, i.v.)abolished the rigidity of the midcollicular decerebrate cat. Mean arterial blood pressure was initially depressed in all animals (0.125-2mg/kg) with an intact medullary vasomotor outflow. Larger doses (4-16mg/kg) tended to return the blood pressure toward control levels. The present study presents evidence for both a brain stem reticular and a spinal cord site of action of diazepam on motor systems. Possible mechanisms of action of diazepam on motor systems are discussed. 16 references. (author abstract)

080144 Weischer, Marie-Luise; Opitz, K. Institut fur Pharmakologie und Toxikologie der Universitat Munster, 44 Munster/Westphalia, Westring 12, Germany /Reduction of analgesic effects by lithium./ Abschwachung analgetischer Effekte durch Lithium. *Arzneimittel-Forschung (Aulendorf).* 20(8):1046-1048, 1970.

Pretreatment with lithium chloride (40meq/1 in drinking water, 8 days) greatly reduced the analgesic effects of codeine, dextropropoxyphene, and glafenine in mice. It is suggested that lithium impairs the response to analgesics by altering the metabolism of monoamines in brain. 13 references. (author abstract)

080336 Brimijoin, Stephen; Pluchino, Salvatore; Trendelenburg, Ullrich. National Institute of Mental Health, Section on Pharmacology, Building 10, Room 2D-4F, Bethesda, Maryland 20014 On the mechanism of supersensitivity to norepinephrine in the denervated cat spleen. *Journal of Pharmacology and Experimental Therapeutics.* 175(2):503-513, 1970.

The mechanism of denervation supersensitivity to norepinephrine was tested by a series of parallel experiments on the cat spleen. Uptake was measured as the removal of norepinephrine from

the perfusate. Sensitivity was assessed both in the whole spleen, in situ, and in the isolated spleen strip. Tissue norepinephrine was measured in each spleen. A sharp fall in uptake and tissue norepinephrine began about 48 hours after the removal of the left celiac ganglion and reached a minimum about 48 hours later, while a 20 fold increase in sensitivity to norepinephrine occurred over the same time period. Sensitivity was approximately related to the logarithm of uptake. A rational model, developed from simple assumptions about the distribution of drug between bathing fluid and site of action, and about the kinetics of uptake by nerves, is the basis of an equation that predicts the experimental relation between uptake and sensitivity. This strongly argues that reduction in uptake causes the rapidly developing component of denervation supersensitivity to norepinephrine in the cat spleen. 33 references. (Author abstract)

080352 Axelrod, Julius; Mueller, Robert A.; Thoenen, Hans. National Institute of Mental Health, Department of Health, Education and Welfare, Bethesda, Maryland 20014 Neuronal and hormonal control of tyrosine hydroxylase and phenylethanolamine N-methyltransferase activity. ***In: Bayer-Symposium II.*** **Springer-Verlag, 1970. (p. 212-219).**

Neuronal and hormonal control of tyrosine hydroxylase and phenylethanolamine N-methyltransferase (PNMT) activity is reviewed and discussed. From the observations made here, it is apparent that the 2 enzymes have similar control mechanisms for their induction and maintenance. The normal levels of PNMT in the adrenal gland are maintained by corticotropin (ACTH) and glucocorticoids, while those of tyrosine hydroxylase are maintained by ACTH. Both enzymes are elevated above normal levels by increased nerve stimulation, tyrosine hydroxylase being quantitatively more affected than PNMT. 29 references. (Author abstract modified)

080606 Beach, Frank A. Department of Psychology, University of California, Berkeley, California 94720 Coital behavior in dogs: VI. long-term effects of castration upon mating in the male. ***Journal of Comparative and Physiological Psychology (Monograph).*** **70(3):1-32, 1970.**

Seven sexually experienced male dogs were castrated and tested for copulatory behavior for 21 to 36 months. Gonadectomy had no effect upon latency or rate of mounting behavior. Within 6 months after operation there was a decrease in the frequency of intromission and in the length of time erection was maintained as reflected by duration of the copulatory lock. These behavioral measures showed no further decline in 2.5yr. Administration of testosterone propionate temporarily reversed the changes produced by castration. Castrated males without androgen therapy continued to display the complete copulatory pattern after adrenalectomy. Two males castrated at 4 mo. of age showed normal mounting responses, and under the influence of exogenous androgen achieved intromission. They were unable to effect complete mating with a genital lock and this probably was due to underdevelopment of the penis. Three males without coital experience were castrated at 30 mo. of age and tested with estrous females 6 mo. later. The dogs were emotionally disturbed by the novel testing situation and relatively little mounting behavior occurred. Administration of testosterone propionate was followed by the display of completely normal copulatory behavior on the part of all castrates. Three months after cessation of androgen therapy only one completed mating occurred but mounting responses continued well above pretreatment levels. 61 references. (Author abstract)

080634 Wittrig, John; Woods, A. E.; Anthony, E. J. Murfreesboro Veterans Administration Hospital, Murfreesboro, Tennessee Mechanisms of lithium action: (endogenous tissue levels, excretion in emotional states, and behavioral effects). ***Diseases of the Nervous System.*** **31(11):767-771, 1970.**

The possible roles of mechanisms of action which endogenous and exogenous lithium may play in either normal or abnormal physiological and psychological processes in rats, rabbits and man have been investigated and some of the major findings are reported. Data on endogenous tissue levels, excretion in emotional states, and behavioral effects of lithium are presented. Problems in methodology are discussed. Two points of caution are extended for studies of endogenous lithium: 1) glassware of the chemically hardened variety is a potential contaminant, and 2) the water supply in any endogenous study is a potential source of extreme variability. The data obtained in these studies indicate that lithium is present in biological tissue in widely varying amounts. There are many hazards and pitfalls for those attempting to measure lithium, but a picture

is beginning to emerge of some meaningful inequalities in the distribution of endogenous lithium in mammaliam tissue with high concentrations being found in endocrine and reproductive systems. Pharmaceutical lithium has little effect on standard behavioral measures of laboratory rats, but it may interact differentially with hormonal substances in the animals. 8 references.

081063 Banna, N. R.; Jabbur, S. J. Department of Pharmacology School of Pharmacy, American University of Beirut, Beirut, Lebanon Increased transmitter release induced by convulsant phenols. *Brain Research (Amsterdam).* 20(3):471-473, 1970.

Adult spinal cats with dorsal root - ventral root preparations in the lumbosacral region were used to test the spinal neurophysiological effect of convulsant phenols (phenol 5mg/kg, catechol 3mg/kg, pyrogallol 7mg/kg, and 4-fluorophenol 4mg/kg). All the phenolic substances tested produced an immediate increase in the size of the monosynaptic response (MSR) after i.v. administration. The increase was more pronounced in preparation where the control MSR was below 1mV. Recovery was observed 20 to 40 min after administration. Qualitatively similar results were obtained after stimulation of extensor or flexor nerves. The polysynaptic response obtained after stimulation of the sural nerve was also increased in size. The stimulus - response delay of the MSR was decreased by about 0.20msec. Methysergide andchlorpromazine had no effect on these facilitatory effects of the phenols. It was also found that this synaptic facilitation could also be produced in both excitatory and inhibitory synapses. These results are consistent with the theory that convulsant phenols may act centrally by increasing the amount of transmitter released by nerve impulses, thus amplifying excitatory as well as inhibitory synaptic transmission. 10 references.

081065 Gonne, L.-M.; Jonsson, J.; Fuxe, K. Psychiatric Research Center, Ulleraker Hospital, S-750 17 Uppsala, Sweden Effects of chronic morphine administration on the catecholamine depletion induced by reserpine. *Journal of Pharmacy and Pharmacology (London).* 22(7):550-552, 1970.

Male white Sprague-Dawley rats given morphine HC1 (increasing doses up to 180mg/kg i.p. b.i.d. for 3 weeks) and reserpine (5mg/kg i.p.)4 hours after the morning morphine dose only, were used. In control rats there was a rapid and profound depletion of noradrenaline to 11% of the starting concentration; this depletion lasted longer than in morphine treated rats. At 72 hours after reserpine injection, the noradrenaline concentration was still 26% of normal in the controls. Continuous administration of morphine reduced the degree of depletion. The noradrenaline level was 59% at 12 hours after reserpine and 48% at 48 and 72 hours. In withdrawal rats not given morphine after the reserpine, the noradrenaline concentrations were also higher than in controls (45% at 28 hours and 75% at 48 hours after reserpine). A corresponding pattern was obtained in brain dopamine. In morphine tolerant animals, dopamine depletion was only moderate, with concentrations remaining between 43% and 75%of the starting value. Dopamine concentrations in the withdrawal group returned to normal sooner than did noradrenaline. Histochemical studies showed a catecholamine depletion after reserpine within cell bodies and terminals only in the controls rats. 11 references.

081106 Marcucci, F.; Fanelli, R.; Mussini, E.; Garattini, S. Istituto di Ricerche Farmacologiche 'Mario Negri', Via Eritrea, 62, 20157, Milan, Italy Further studies on the long lasting antimetrazol activity of diazepam in mice. *European Journal of Pharmacology (Amsterdam).* 11(1):115-116, 1970.

Male Albino Swiss mice were used to study the long lasting antimetrazol activity of diazepam. After various tentative preliminary trials, a procedure was found whereby similar levels of brain oxazepam could be obtained after administration of diazepam or oxazepam. Levels over 0.06 microgram per gram of brain oxazepam were necessary to afford significant protection against metrazol. Levels around 0.15 microgram per gram of brain oxazepam obtained either after i.v. administration of diazepam or oxazepam permit a protection of about 80%. N-demethyldiazepam or N-methyloxazepam were not present in mice brain 20 hours after diazepam administration within the limits of the sensitivity of the method. It may be concluded that diazepam exerts its long lasting anticonvulsant effect in mice through the accumulation of brain oxazepam. 6 references.

081111 Krulik, R.; Zvolsky, P. Author address not given The effect of lithium on the metabolism of experimental animals. *Activitas Nervosa Superior (Praha).* 12(3):279-283, 1970.

After a single oral application of 5 millimoles lithium chloride (LiCl) per kg we failed to observe

any significant changes after 5 hours either in the serum levels of glucose and nonesterified fatty acids or in the liver pyruvic and alpha-ketoglutaric acids. Application of 25 millimoles LiCl/kg/day lasting 1 week caused the increase of glucose by about 21 percent. The level of serum nonesterified fatty acids did not change, but the levels of pyruvic and alpha-ketoglutaric acids increased significantly. The application of 1 and 2 millimoles LiCl/kg/day which lasted 10 days led to a decrease of the levels of triglycerides in liver tissue and to an increase of glycogen in comparison to the control groups. 25 references. (author abstract)

081112 Sheard, Michael H. Department of Psychiatry, Yale University School of Medicine, New Haven, Connecticut Behavioral effects of p-chlorophenylalanine in rats: inhibition by lithium. ***Communications in Behavioral Biology.*** **5(2):71-73, 1970.**

Male Sprague-Dawley rats were treated with lithium chloride or physiological saline for 5 days. On day 4 they were given p-chlorophenylalanine (PCPA) and 15 to 24 hr later their behavior was rated in an observation chamber. There was a significant inhibition of PCPA to induced sexual and aggressive behavior in the lithium - pretreated animals with an increase in resting behavior. After PCPA, 5-hydroxyindoleacetic acid levels were lower in the forebrain in lithium treated animals than in saline treated animals. 9 references. (author abstract)

081151 Anden, N. -E.; Corrodi, H.; Fuxe, K.; Hokfelt, B.; Hokfelt, T.; Rydin, C.; Svensson, T. Department of Pharmacology, University of Goteborg, S-400 33 Goteborg 33, Sweden Evidence for a central noradrenaline receptor: Stimulation by clonidine. ***Life Sciences (Oxford).*** **9(9):513-523, 1970.**

Clonidine increased the flexor reflex of spinal rats after depletion of all known noradrenaline stores, indicating a stimulation of central noradrenaline receptors. No stimulation of 5-hydroxytryptamine or dopamine receptors was observed. The motility of reserpine treated animals was enhanced by clonidine provided that the dopamine receptors were stimulated. Clonidine reduced the disappearance of noradrenaline and also that of 5-hydroxytryptamine after synthesis inhibition. The chemical effects might be due to a negative feedback mechanism, evoked by the noradrenaline receptor stimulation. Both the functional and chemical changes were reduced by the noradrenaline receptor blocking agents haloperidol and phenoxybenzamine. 25 references. (author abstract)

04 MECHANISM OF ACTION: BEHAVIORAL

075844 Richter, Judith A.; Goldstein, Avram. Department of Biochemistry, University of Cambridge, Cambridge, England The effects of morphine-like compounds on the light responses of the brine shrimp Artemia salina. ***Psychopharmacologia (Berlin).*** **17:327-337, 1970.**

Studies on the effects of morphinelike compounds on the light responses of the brine shrimp, Artemia salina, were made after methods for the measurement of light responses of Artemia nauplii and adults were developed. The methods are described. Application of the methods gave the following results: although no effects of levorphanol were found on the positive phototaxis of nauplii, this compound inhibited and partially reversed the negative phototaxis of adults. Levorphanol was also effective in adults after removal of the compound eyes, indicating that it probably acts on the median eye or its central connections in adults. Methadone and dextrorphan (the inactive stereoisomer of levorphanol) caused similar effects in adults, but morphine was inactive. Pentobarbital inhibited the negative movement but induced very little positive phototaxis. Attempts to reverse the effect of levorphanol with nalorphine pretreatment was unsuccessful. Attempts to develop tolerance to levorphanol were also unsuccessful; the shrimp died, apparently as a result of an increasing effect of the drug with time. 9 references. (Author abstract modified)

075847 Villablanca, J.; Riobo, F. Catedra de Fisiopatologia, Escuela de Medicina, Casilla 3170, Santos Dumont 999, Santiago, Chile Electroencephalographic and behavioral effects of harmaline in intact cats and in cats with chronic mesencephalic transection. ***Psychopharmacologia (Berlin).*** **17:302-313, 1970.**

The electroencephalographic (EEG) and behavioral effects of threshold doses of harmaline were studied in 4 chronically implanted freely moving intact cats and 5 chronic animals with complete mesencephalic transection. Behaviorally, the drug induced intense motor activation, tonic

postural and gait abnormalities, tremor, abnormal facial expression, crying and neurovegetative phenomena in both intact and physiologically decerebrate cats plus exploratory behavior in intact animals. Paradoxical sleep was suppressed for about 7 hours. Electrocortically, the drug induced intermittent or continuous hypersynchrony which was most predominant over visual areas. In intact cats there was a short desynchronization immediately after the injection and in the 'cerveau isole' the drug induced a 'synchronization period'. The electrocortical synchronization as well as the paradoxical sleep suppressor effects are discussed in the light of the monoamine oxidase inhibiting action of harmaline. The tremorogenic effect is attributed to lower brain stem motor mechanisms and considered to be related to the pontine reticular EEG events. The fact that many of the actions of this hallucinogen can be accounted for without the necessary participation of rostral brain structures is particularly stressed. 17 references. (Author abstract modified)

075848 Clark, Carol V. H. Veterans Administration Hospital, 1055 Clermont Street, Denver, Colorado 80220 Effect of hippocampal and neocortical ablation on scopolamine- induced activity in the rat. ***Psychopharmacologia (Berlin).*** **17:289-301, 1970.**

To test the hypothesis that the hippocampus may be an important site of action for anticholinergic drugs, scopolamine was administered to rats with hippocampal lesions produced by aspiration and to appropriate control groups, and their activity measured. The experimental design was a 4 way analysis of variance with 3 lesion groups, 3 drug levels, 8 measurements in a 2 hour session, and 4 weeks. At the 2 higher drug doses (0.20 and 1.0mg/kg), rats with hippocampal or cortical lesions had significantly greater activity than the sham operates (p less than 0.01 and p less than 0.05, resp.)A group of rats with electrolytic hippocampal lesions tested at 0.20mg/kg scopolamine had transitory activity increases. Therefore the hippocampus is not necessary for the motor activating effects of the drug nor is its ablation unique in producing increases in drug induced activity. 13 references. (Author abstract)

075869 Snyder, Solomon H.; Taylor, Kenneth M.; Coyle, Joseph T.; Meyerhoff, James L. The Johns Hopkins University School of Medicine, 725 North Wolfe Street, Baltimore, Maryland 21205 The role of brain dopamine in behavioral regulation and the actions of psychotropic drugs. ***American Journal of Psychiatry.*** **127(2):199-207, 1970.**

The role of brain dopamine in behavioral regulation and the actions of psychotropic drugs is reviewed. By comparing biochemical and behavioral actions of d- and l-isomers of amphetamine, it is shown that locomotor hyperactivity, an animal model for the central stimulant effects of amphetamine, is mediated by brain norepinephrine. By contrast, stereotyped, compulsive gnawing behavior in rats, which resembles symptoms of amphetamine psychosis, appears to be regulated by brain dopamine. Since haloperidol, a potent blocker of dopamine receptors, is uniquely efficacious intreating Gilles de la Tourette's disease, it is suggested that the hyperactivity of dopamine systems in the brain may be a factor in the pathophysiology of this condition. 84 references. (Journal abstract modified)

075870 Hines, Garth; Lee, Andrew E.; Miller, William T. University of Montana, Missoula, Montana 59801 Effect of atropine dose level on the suppression of water-reinforced VI responding. ***Psychonomic Science.*** **20(1):37-38, 1970.**

Rats trained to barpress on a variable interval (VI, 1 min schedule for water reinforcement received 4 dose levels (1.0, 2.0, 4.0, and 8.0mg/kg) of atropine sulfate or atropine nitrate. Compared with saline injected controls, increasing doses of atropine sulfate resulted in increasing degrees of response suppression. The same result was obtained with atropine methyl nitrate, although to a lesser degree. It was suggested that the failure to obtain extensive response facilitation at the lower dose levels of atropine methyl nitrate may have been due to the existence of a limit to the operating capacity of the central thirst system. 13 references. (Author abstract)

075882 Powell, Barbara J. Malcolm Bliss Mental Health Center, 1420 Grattan Street, St. Louis, Missouri 63104 The role of d-amphetamine-amobarbital in suppressing freezing behavior during avoidance acquisition and extinction. ***Psychological Record.*** **20(1):101-105, 1970.**

The effects of a combined dosage of d-amphetamine sulfate and amobarbital sodium on the freezing behavior of rats during avoidance acquisition and extinction are investigated. The

drug combination increased avoidance acquisition and suppressed freezing; however, withdrawal of one or both drugs during extinction resulted in differential performance, suggesting that drug effects were 'state dependent.'16 references. (Author abstract)

075890 Beatty, William W.; Beatty, Patricia Ann. North Dakota State University, Fargo, North Dakota 58102 Effects of neonatal testosterone on the acquisition of an active avoidance response in genotypically female rats. ***Psychonomic Science.*** **19(5):315-316, 1970.**

A study is reported of the effects of neonatal testosterone on the acquisition of an active avoidance response in genotypically female rats. The rats received either testosterone or placebo injections at 3 days of age and ovariectomy plus placebo, ovariectomy plus estrogen, or ovariectomy plus testosterone treatments in adulthood. Females that received testosterone both in infancy and in adulthood exhibited the inferior avoidance performance typical of normal males; the other 7 groups behaved like untreated females. Testosterone appears to organize neural mechanisms responsible for sex differences in avoidance behavior, but additional androgenic stimulation is required for the expression of masculine avoidance behavior. 11 references. (Author abstract modified)

075891 Branchey, Marc; Kissin, Benjamin. State University of New York, Downstate Medical Center, Brooklyn, New York 11203 The effect of alpha-methyl-para-tyrosine on sleep and arousal in the rat. ***Psychonomic Science.*** **19(5):281-282, 1970.**

A single intraperitoneal injection of 200mg/kg of body weight of dl-alpha-methyl-para-tyrosine in the rat induced a significant increase in nonrapid eye movement (NREM) sleep without affecting rapid eye movement (REM) sleep. The rats were implanted with cortical, subcortical, and muscular electrodes. The results support the hypothesis of the existence of a catecholaminergic mechanism of arousal. 22 references. (Author abstract)

075906 Marr, M. Jackson. School of Psychology, Georgia Institute of Technology, Atlanta, Georgia 30332 Effects of chlorpromazine in the pigeon under a second-order schedule of food presentation. ***Journal of the Experimental Analysis of Behavior.*** **13(3):291-299, 1970.**

Chlorpromazine was studied for its effects on responding under a second order schedule in which food was presented to pigeons following a sequence of 20 one minute fixed interval components. A brief visual stimulus occurred at the completion of each fixed interval including the one that terminated with food presentation. Chlorpromazine showed rate dependent effects in that it increased low rates in the early components of the second order schedule and, to a lesser extent, decreased high rates in the later components. Chlorpromazine also increased rates in the early quarters within the 1 min fixed internal components and to a smaller extent decreased rates in the final quarter. The alteration in the patterns of responding within 1 min fixed interval components terminating in a brief stimulus presentation was substantially less than that which occurred throughout the succession of 1 min fixed interval components terminating in food presentation, thus suggesting that the presentation of brief stimulus exerted more control over responding within components than did food presentation over the sequence of components. This result and others suggest that studies using drugs may be useful in elucidating the factors controlling patterns of responding in second order schedules. 23 references. (Author abstract)

075915 Weisinger, Richard S.; Woods, Stephen C.; Skorupski, Joseph D. Department of Psychology, University of Washington, Seattle, Washington 98105 Sodium deficiency and latent learning. ***Psychonomic Science.*** **19(5):307-308, 1970.**

A study is reported of the relationship between sodium deficiency and latent learning. Rats were trained to press a lever toobtain a 0.33 M saline solution while thirsty. Later, under extinction conditions, those rats that had been injected with either formalin or aldosterone pressed a significantly higher percentage of their former rates than did their respective controls. Formalin has been shown to make rats hyponatremic in this situation, while aldosterone makes them slightly hypernatremic. Yet both drugs elicit sodium appetite. Therefore, sodium appetite, rather than hyponatremia, is postulated to be the condition necessary to demonstate this enhanced barpressing, a form of latent learning. 9 references. (Author abstract modified)

075917 Glick, S. D.; Jarvik, M. E.; Levin, B.; Carley, J. L. Department of Pharmacology, Albert

Einstein College of Medicine, Yeshiva University, 1300 Morris Park Avenue, Bronx, N. Y. 10461 An automated multiple choice test of short-term spatial memory for monkeys. *Journal of the Experimental Analysis of Behavior.* 13(3):317-318, 1970.

An automated multiple choice test of short-term spatial memory for monkeys is described. Since Hunter developed the delayed response test in 1913, it has been widely used in the study of memory, brain damage, and behavioral pharmacology. A major problem is that the usual dichotomous choice method allows the animal a 50% chance of being correct on any trial. Thus, it is necessary to average the results of many animals or many trials to obtain a reliable measure of accuracy. A few investigations (e.g.,Riopelle, 1959) have utilized manual multiple choice delayed response procedures, but these have been tedious to conduct and have not provided a measure of the degree of error. The present multiple choice procedure was designed to provide a semiquantitative measure of the degree of error on a single trial. 3 references.

075922 Burkman, A. M. Division of Pharmacology, College of Pharmacy, Ohio State University, Columbus, Ohio 43210 Automatic monitoring of apomorphine-induced pecking in pigeons. *Journal of the Experimental Analysis of Behavior.* 13(3):349-350, 1970.

This technical note discusses automatic monitoring of apomorphine induced pecking in pigeons. Compulsive pecking, provoked by apomorphine and related drugs, has been the subject of considerable interest to pharmacologists as a model of drug induced stereotypical behavior. The total number of pecks during the period of drug action (cumulative pecks) has proved to be the most useful parameter of response, as it represents a reliable measure of dose dependent response intensity. The design of an electromechanical monitor for recording pecking is discussed and diagrammed. A 6 channel unit has been in use for approximately 2 years and, during that time, has functioned effectively and efficiently as an attendant free assay instrument. 5 references.

075996 Wilson, Wendell L.; Darcy; John M.; Haralson, John V. University of Washington, Seattle, Washington 98105 Reserpine and conditioned suppression in the fish Tilapia h. macrocephala. *Psychonomic Science.* 30(1):47-49, 1970.

African mouthbreeding fish were trained to strike a bar on a VR2 schedule of reinforcement. Over a 10 day period, operant rate of responding was measured on 5 days, randomly interspersed with 5 days on which light (CS) was followed by shock (US) on 10 trials per day in the same environment. The CS was later introduced during operant responding; this resulted in suppression of operant responding. Subsequent injection of reserpine attenuated suppression of operant responding, but saline injection did not. These results probably were a direct function of reserpine administration on rate of recovery of responding following CS onset rather than an indirect function of baseline response rate or 'sedation effects.'19 references. (Author abstract)

076066 Dyne, Lesley J.; Hughes, R. N. University of Canterbury, Christchurch, New Zealand Effects of methylphenidate on activity and reactions of novelty in rats. *Psychonomic Science.* 19(5):267-268, 1970.

Rats injected with 4.0or 8.0mg/kg of methylphenidate prior to observation in a 4 cell exploration box showed a significant preference for the less novel half of the apparatus and a reduction in eating and drinking compared with control animals injected with sterile water. The higher dosage also decreased freezing behavior but increased sniffing and the total number of cells entered. While confirming some previous findings, the results emphasized the need in drug studies for distinguishing between exploratory responses directed towards novel environmental stimuli and randomized, nondirected general activity. 8 references. (Author abstract)

076080 Wade, George N.; Zucker, Irving. Department of Psychology, University of California, Berkeley, California 94720 Modulation of food intake and locomotor activity in female rats by diencephalic hormone implants. *Journal of Comparative and Physiological Psychology.* 72(2):328-336, 1970.

Estradiol benzoate (EB), unilaterally implanted in the vicinity of the ventromedial hypothalamus (VMH) significantly depressed food intake of spayed female rats within 12 hr. of application. This effect was similar in magnitude to changes in eating following systemic injections of EB. The EB placements in the lateral hypothalamic area (LHA) and anterior hypothalamus preoptic area (AH-POA) were far less effective in influencing

food intake. The EB stimulation of the POA greatly increased locomotor activity, while LHA and VMH implants were without effect. Implants near the arcuate nucleus depressed activity. The effects of progesterone, testosterone, and cholesterol at these loci are also described. The neuroendocrine control of energy balance is discussed; it is concluded that estrogens act on separate diencephalic regions to modualate energy intake and energy expenditure. 23 references. (Author abstract)

076081 Levitt, Robert A.; White, Carol Sue; Sander, Don M. Department of Psychology, Southern Illinois University, Carbondale, Illinois 62901 Dose-response analysis of carbachol-elicited drinking in the rat limbic system. *Journal of Comparative and Physiological Psychology.* 72(2):345-350, 1970.

An experiment is described which reports on dose response analysis of carbachol elicited drinking in the rat limbic system. Water intake and latency to drink elicited by 5 doses of carbachol at 63 loci located throughout the rat limbic system were determined. About × of the sites were stimulated by carbachol in crystalline form; for the others the carbachol was in solution. The major differential effect was that animals receiving the solution began drinking in about 3× min.,whereas those stimulated with crystals began in about 6× min. No differences in effect between widely divergent limbic system locations were found on drinking volume, latency, or threshold. Distance to the nearest ventricle was also not a critical factor. The data suggest a diffusely organized cholinergic system involved in the elicitation of drinking and located throughout the limbic system. 9 references. (Author abstract modified)

076086 Green, Richard; Luttge, William G.; Whalen, Richard E. Department of Psychobiology, University of California, Irvine, California 92664 Uptake of tritiated testosterone in brain and peripheral tissues of normal and neonatally androgenized female rats. *Journal of Comparative and Physiological Psychology.* 72(2):337-340, 1970.

An investigation is reported on uptake of tritiated testosterone in brain and peripheral tissues of normal and neonatally androgenized female rats. Ovariectomized female rats treated with testosterone propionate or oil in infancy were administered tritiated testosterone subcutaneously (SC) or intravenously (IV) in adulthood to test the hypothesis that early androgenization alters the ability of hormone target tissues to accumulate radioactivity. Samples of hypothalamus, preoptic diagonal band region, cortex, pituitary, uterus, and muscle, were taken 20 min. after injection of 1, 2-H-testosterone. The data indicated selective accumulation of radioactivity levelsafter IV than SC administration, but no significant differences in accumulation of radioactivity between normal and neonatally androgenized females. 13 references. (Author abstract)

076131 Thor, Donald H.; Hoats, David L. E. R. Johnstone Training and Research Center, Bordentown, New Jersey 08505 Morphine-amphetamine-induced fighting and interim socialization. *Psychonomic Science.* 20(3):156-158, 1970.

Traumatic and lethal fighting among male rats can be induced by a single moderate dose of amphetamine given during withdrawal from morphine. Socialization with other rats during the interval between terminal morphine and amphetamine modifies the course of subsequent aggressive behavior. Fighting is prolonged for rats maintained in isolation during the interdrug interval. 10 references. (Author abstract)

076133 Potts, W. Joseph; Morse, David L.; Cooper, Barrett R.; Black, William C. Department of Pharamcology, G. D. Searle & Co., P. O. Box 5110, Chicago, Illinois 60680 The effect of magnesium pemoline, tricyanoaminopropene and d-amphetamine on discriminated avoidance performance in rats as a function of age. *Psychonomic Science.* 20(3):141-143, 1970.

The effects of magnesium pemoline, tricyanoaminopropene, and d-amphetamine on the acquisition of a discriminated avoidance response are compared in 30, 50, and 100 day-old rats. The rats were placed in an automated shuttlebox immediately after drug treatment. The number of avoidance responses in a series of 100 trials was measured. Ten days after the initial acquisition session, the rats were retrained on the same task. The 30-day group was inferior to the 50- and 100-day groups in the training session, but no differences occurred in retraining. The drug-treated groups showed improved performance in the initial training session b mu were not different from the controls in the retraining session. No drug by age interaction was significant. 26 references. (Author abstract)

076164 Pishkin, Vladimir; Rasmussen, Elizabeth A.; Duke, Carla R. University of Oklahoma School of Medicine, Oklahoma City, Oklahoma 73104 Hydroxyzine and shock in operant behavior of rats. ***Psychonomic Science.*** **20(3):175-176, 1970.**

A total of 25 shaped or unshaped water deprived rats injected with either saline or hydroxyzine hydrochloride performed on a barpressing task. Unavoidable shock was provided throughout the experimental procedure. Hydroxyzine rats outperformed their saline counterparts. Although there were no differences between the groups on the final shaping trial, the hydroxyzine rats maintained significantly higher levels of performance than the saline rats under shock conditions. 4 references. (Author abstract)

076213 Beck, Charles H.; Chambers, W. W. Department of Psychology, University of Alberta, Edmonton, Alberta, Canada Speed, accuracy, and strength of forelimb movement after unilateral pyramidotomy in rhesus monkeys. ***Journal of Comparative and Physiological Psychology (Monograph).*** **70(2):1-22, 1970.**

Rhesus monkeys showed normal postoperative reaction times (RT) following unilateral section of the medullary pyramids. However, a slowness in RT of the forelimb contralateral to the lesion appeared in 2 choice RT tasks in which no choice resolving pretrial cues were present in the environment. Pyramidotomized monkeys had no difficulty in stopping a movement quickly and accurately at a specified point in space. The impaired forelimb exhibited a greater loss of strength in flexion than in extension. The weakness in flexion was greater at the wrist than at the elbow or shoulder. The percentage of pyramidal tract destroyed correlated significantly with the severity of the strength deficit. Amphetamine injections temporarily ameliorated the contact placing reaction deficit of the pyramidal limb. 27 references. (Author abstract)

076316 Kircher, Karen A.; Braun, J. Jay; Meyer, Donald R.; Meyer, Patricia M. Lab. for Comp. and Physiol. Psych., Ohio State Univ. Research Center, Area 2, 1314 Kinnear Road, Columbus, Ohio 43212 Equivalence of simultaneous and successive neocortical ablations in production of impairments of retention of black-white habits in rats. ***Journal of Comparative and Physiological Psychology.*** **71(3):420-425, 1970.**

An experiment is presented which evaluates the equivalence of simultaneous and successive neocortical ablations in the production of impairments of retention of black/white habits in rats. The rats subjected to a 2 stage removal of the posterior or anterior isocortex retained a black/white habit no better than 1 stage bilateral control animals. Amphetamine injections combined with light and dark housing conditions during the interoperative interval also failed to yield savings. The 2 reported experiments suggest that successive procedures which do not involve interoperative training and unlikely to produce improved retention of a black/white habit. 13 references. (Author abstract modified)

078402 Appel, James B. University of Chicago, Chicago, Illinois 60637 The effects of drugs on continuous avoidance behavior with a warning stimulus. Research Report, NIMH Grants MH 13186, MH-9355, 1970.

The effects of lysergic acid diethylamide (LSD), chlorpromazine (CPZ) and d-amphetamine on continuous (Sidman) avoidance behavior with a warning stimulus (light and buzzer) were compared. While relatively high doses of LSD (0.32 - 1.28 mg/kg) depressed the overall rate of the wheel turning avoidance response, only 1.28 mg/kg affected efficient responding, i.e.,responding in the presence of the warning stimulus. CPZ had a greater depressing effect on efficient responding than it did on overall rate and d-amphetamine increased the total amount of avoidance behavior. The effects of all of the drugs were similar to those obtained in the same apparatus in discrete trial escape and avoidance situations. 11 references. (Author abstract)

079888 Willner, Joseph H.; Samach, Michael; Angrist, Burton M.; Wallach, Marshall B.; Gershon, Samuel. Neuropsychopharmacology Research Unit, Department of Psychiatry, New York University Medical Center, 550 First Avenue, New York, New York Drug-induced stereotyped behavior and its antagonism in dogs. ***Communications in Behavioral Biology.*** **5(3):135-141, 1970.**

Pharmacologically induced stereotyped behavior in dogs was explored as a model for paranoid psychoses induced by certain stimulants in man. Conscious, free moving dogs were administered various agents in order to induce stereotype. Cocaine, d-amphetamine, and L-dihydroxyphenylalanine induced stereotyped behavior. Antagonism of this behavioral pattern by haloperidol and chlorpromazine was assessed. Haloperidol

was less sedative and more effective than chlorpromazine. Other psychotomimetics and stimulants which did not elicit stereotype included 5-hydroxytryptophan, mescaline, and caffeine. Clinical and neurochemical correlations are discussed. 38 references. (Author abstract)

079970 Saavedra, J. M.; Fischer, E. Hospital Nacional Jose T. Berda (Ex-Neuropsiquiatrice de Hombres), Barracas (Ex Vieytes) 375, Buenos Aires, Argentina Antagonism of beta-phenylethylamine derivatives and serotonin blocking drugs upon serotonin, tryptamine and reserpine behavioral depression in mice. *Arzneimittel-Forschung (Aulendorf).* 20(7):952-957, 1970.

When injected i.p. to mice, tryptamine, 5-hydroxytryptamine and reserpine produce a similar locomotor depression, quantitatively measured in the actophotometer. The antiserotonin drugs methysergide and LSD completely blocked both the tryptamine and reserpine effects; they did not reverse the serotonin locomotor depression, although the animals became behaviorally excited. The monoamine oxidase inhibitor iproniazid potentiates the tryptamine effect, has no action upon serotonin and reverses the reserpine syndrome when injected first. Tranylcypromine blocked the depressant effects of tryptamine, serotonin and reserpine. Methylamphetamine and beta-phenylethylamine also completely blocked these depressive effects. A physiological role for both tryptamine and beta-phenylethylamine as neurohumoral agents is postulated. 65 references. (author abstract)

079982 Nordgren, Richard A.; Woodruff, Diana S.; Bick, Michael D. Department of Biological Sciences, Gerontology Center, University of Southern California, Los Angeles, California 90007 The effect of exogenous RNA on the retention of discriminative learning in the rat. *Physiology and Behavior.* 5(10):1169-1171, 1970.

To test the hypothesis that administration of RNA affects behavior by providing a supply of precursors for de novo synthesis of RNA, the effect of whole RNA was compared to that of an alkaline hydrolysate. Twenty eight male rats were trained on a discriminationtask and divided into 4 groups of equal mean performance on the task. Each group received 1 of the following treatments: whole RNA injection, hydrolysate RNA injection, saline injection, no injection. No significant difference was observed in the mean performance of the 4 groups after the injections. Thus, RNA did not affect learning or retention of a discrimination task. Since the procedure of some experiments demonstrating the positive effect of RNA on learned behavior was to repeatedly inject animals with RNA over long periods of time while the procedure in the present study was to inject the animals once, the difference in results may have been due to experimental differences in the injection schedule. 8 references. (author abstract)

079998 Hingtgen, J. N.; Aprison, M. H. Institute of Psychiatric Research, Indianapolis, Indiana Increased duration of neuropharmacologically induced behavioral excitation by atropine. *Neuropharmacology (Oxford).* 9(5):419-425, 1970.

Acetylcholine has been implicated as an important factor in the production of behavioral excitation in rats working on avoidance schedules and injected with tetrabenazine following iproniazid pretreatment. To further study the role of acetylcholine in this type of behavior, an anticholinergic drug, atropine, was injected into iproniazid - tetrabenazine treated avoidance rats. When small doses of atropine (0.1-0.2mg/kg) were given 60-120 min before 2mg/kg tetrabenazine (50mg/kg iproniazid was always given 18 hr before tetrabenazine), the duration of behavioral excitation was significantly increased. A larger dose of atropine (0.8mg/kg) blocked behavioral excitation. Comparable doses of methyl atropine nitrate had no effect on excitation. These results support our previous hypothesis that acetylcholine is involved in excited states of avoidance behavior. In addition, the extended behavioral excitation seen after low doses of atropine suggest that this drug can cause either a release of acetylcholine or prevent its uptake into the presynaptic or postsynaptic neurons of cholinergic synapses. 17 references. (author abstract modified)

079999 Stolerman, I. P. Department of Pharmacology, University College, London, England Eating, drinking and spontaneous activity in rats after the administration of chlorpromazine. *Neuropharmacology (Oxford).* 9(5):405-417, 1970.

Previous studies of the effects of chlorpromazine on eating and drinking gave conflicting results. The experiments described here show that chlorpromazine can have a biphasic time course of action in rats, and that if this is taken into account, some of the apparently discrepant findings

can be reconciled. For about 2 hr after administration, all the doses tested reduced food intake, but after that, the same doses stimulated eating. The long-term increases in food intake seem consistent with most of the clinical literature. Rats given limited amounts of food to eat each day showed less clear stimulant responses than those allowed to eat for limited periods of time each day. Furthermore, records of spontaneous activity suggested that some form of generalized depression of behavior might partly mask underlying stimulant effects on eating. Complex changes in hunger and thirst may therefore occur for several hours after chlorpromazine is given and these may be particularly important when food and water are used as rewards in experiments involving learning. 47 references. (author abstract)

081066 Schnieden, H.; Truslove, Gillian M. Department of Pharmacology, University of Manchester, England The effect of some drugs on genetic tremor in the mouse. ***European Journal of Pharmacology (Amsterdam).*** **11(1):33-37, 1970.**

Mice with congenital tremor (trm) were used to determine the effect of drugs on their abnormal behavior. The typical behavior of the mice prior to drug administration was a marked reluctance to move about and explore a new environment, a sudden attack of trembling (especially after any disturbance) and a characteristic walk. Their gait was lurching and they appeared to lift their hind legs too high off the ground. At birth the trm mice were lighter than their littermates and this difference usually persisted throughout life. Drug trials for effect on the trm were conducted. Hycosine hydrobromide (10mg/kg i.p.)was ineffective over a 1 hour period; at 30mg/kg the tremor was diminshed after 10 minutes and persisted for an hour after injection. Atropine sulfate (15mg/kg) had no effect after one hour. Orphenadrine hydrochloride (30mg/kg) significantly depressed the tremor 10 and 15 minutes after injection but was insignificant after 20 minutes. Hexobarbitone, phenobarbitone, nethalide and alpha-methyldopa were ineffective. Anesthesia in 4 animals depressed the tremor, which reappeared after anesthesia. Transection of the thoracic spinal cord in 2 animals with head and body tremor produced a disappearance of tremor below the site of section upon recovery from anesthesia; head tremor was still present. The latter observation suggests that the trm is centrally mediated the specific etiology the trm is unknown. 9 references.

081098 Fox, K. A.; Tuckosh, J. R.; Wilcox, A. H. Department of Biology, State University College, Fredonia, New York Increased aggression among grouped male mice fed chlordiazepoxide. ***European Journal of Pharmacology (Amsterdam).*** **11(1):119-121, 1970.**

The effects of chronic low dose chlordiazepoxide treatment upon aggressive behavior was investigated in male mice. In the first of two experiments, 4 control mice were grouped with 4 mice placed on a chlordiazepoxide supplemented diet for 6 days in a cage and their behavior was observed during the following 40 minutes. These animals remained grouped for 2 weeks and were maintained on there respective diets. Males receiving chlordiazepoxide fought more during the 40 minute observation period than controls. This was reflected in the significant higher mortality rate of experimental animal during the 2 weeks in the group. In the second experiment, 20 control and 20 experimental mice were grouped for an eight week period and maintained on their respective diets. During this period 35 percent of the chlordiazepoxide fed males succumbed, while only 10 percent of the control males died. The ad libitum doses of chlordiazepoxide used in this study which in increased aggression were smaller than doses used in previous studies which have indicated that chlordiazepoxide reduces aggression in mice. 9 references.

081149 Whishaw, Ian Q.; Cooper, R. M. University of Western Ontario, London, Ontario, Canada Strychnine and suppression of exploration. ***Physiology and Behavior.*** **5(6):647-649, 1970.**

Rats under the influence of strychnine were given 20 trials on a very simple Hebb-Williams maze problem and 6 days later, were given a further 20 trials on the same problem when they were not under the influence of the drug. On the drug day, the experimental animals made fewer errors than the control animals, but on the retention test without the drug, the difference was not upheld. These results were taken to mean that strychnine can suppress exploration in maze tasks. This was supported in a second experiment. Maze adapted rats were given an exploratory test which allowed them to take either a familiar route or a number of alternate routes to the goal. Animals injected with strychnine took the familiar route while control animals explored the maze. 8 references. (author abstract modified)

081159 Sayler, Anne. Department of Zoology, University of Illinois, Urbana, Illinois The effect of anti-androgens on aggressive behavior in the gerbil. *Physiology and Behavior.* 5(6):667-671, 1970.

The effects of the antiandrogens, cyproterone and cyproterone acetate, on aggressive behavior in the gerbil, Meriones unguiculatus were determined. No changes in aggressive behavior occurred as a result of 21 days of treatment with antiandrogens. However, there was a significant decline in aggression due to castration. Antiandrogen treatment caused regression of the seminal vesicles and the ventral sebaceous glands, and lowering of testicular weight. 18 references. (author abstract modified)

081226 Stern, Jeffrey J. Department of Psychobiology, University of Michigan, Dearborn, Michigan 48128 Responses of male rats to sex odors. *Physiology and Behavior.* 5(4):519-524, 1970.

A series of 4 experiments investigated the responses of Sprague-Dawley male rats to the odors from sexually receptive females. Having established that Sprague-Dawley male rats prefer the odors of estrous females and that the preferences are not a function of the female's movements or sound, the contribution of the various components of the males' copulatory pattern to the development of preferences was examined. The results showed that sexually naive males fail to showa sex odor preference and that mounting experience is sufficient for the preferences to appear. In the investigation of the relationship between the presence or absence of the testes and the sex odor preferences, it was shown that the preferences disappear approximately 3 weeks following castration. Another experiment examined whether neonatal testicular secretions are necessary if the male rat is to display a sex odor preference in adulthood. Following testosterone propionate administration and mounting experience, day 1 castrates showed a sex odor preference. 11 references. (author abstract)

081227 Block, Martin L.; Fisher, Alan E. Department of Psychology, University of Pittsburgh, Pittsburgh, Pennsylvania Anticholinergic central blockade of salt-aroused and derivation-induced drinking. *Physiology and Behavior.* 5(4):525-527, 1970.

Intracerebral injection of micro quantities of methyl atropine nitrate into chronically implanted cannulae significantly reduced water intake of rats following either subcutaneous injection of hypertonic sodium chloride solution or following periods of water deprivation. Control injections had no effect. It is suggested that a central cholinergic mechanism is operative during both salt - aroused and deprivation - induced drinking behavior. 12 references. (author abstract)

081228 Whalen, Richard E.; Hardy, Donna Fitzroy. Department of Psychobiology, University of California, Irvine, California Induction of receptivity in female rats and cats with estrogen and testosterone. *Physiology and Behavior.* 5(4):529-533, 1970.

Adult female rats were ovariectomized. Two weeks later they were divided into 7 groups and treated daily with estradiol benzoate (EB) or testosterone propionate (TP) in the following doses: 0.5micrograms EB; 0.25 micrograms EB; 0.10 micrograms EB; 0.05 micrograms EB; 1000 micrograms TP and 100 micrograms TB. After 30 to 32 days of treatment the animals were sacrificed, the uteri removed and expressed and uterine wet weights taken. All females were tested for behavioral receptivity twice on 2 days each week for 4 to 5 weeks. The mean uterine weight of the intact females was 388.6mg and of females ovariectomized for one month was 91.6mg. Castrated females or those castrated and treated with TP exhibited only vaginal diestrous. Those treated with estrogen daily showed irregular patterns of vaginal cornification. For each EB dose level behavioral receptivity was more intense when the vagina was classified estrus rather than diestrus or proestrus. Females receiving TP were classified disestrus, yet receptivity was displayed under each dose condition. A similar investigation was carried out in cats with the conclusion that sexual receptivity may be induced in the cat and rat by treatment with both estrogen and testosterone. 12 references.

081231 Rosecrans, John A. Department of Pharmacology, Medical College of Virginia, Richmond, Virginia Forebrain biogenic amine function in high and low female rats. *Physiology and Behavior.* 5(4):453-458, 1970.

Female rats selected for high or low activity were administered the amine synthesis inhibitors p-chlorophenylalanine or alpha-methyl-para-tyrosine, and were subjected to ether behavioral or chemical studies. The data indicated that 5-hydroxytryptamine systems were more functional

in the forebrain of high activity rats, while p-chlorophenylalanine was less active behaviorally in these animals. The reverse situation was evident in low activity rats in which forebrain norepinephrine systems appeared more functional, and alpha-methyl-para-tyrosine was similarly behaviorally less active in these latter animals. These experiments indicate a good correlation between activity level and forebrain biogenic amine function in female rats. However, whether these amine systems are directly involved in the control of activity, or whether these changes are the results of these behavioral differences has not been clarified. 19 references. (author abstract)

081233 Edwards, David A. Department of Psychology, Emory University, Atlanta, Georgia Post-neonatal androgenization and adult aggressive behavior in female mice. ***Physiology and Behavior.*** **5(4):465-467, 1970.**

This experiment sought to determine whether chronic, long-term administation of testosterone propionate to post-neonatal female mice would facilitate the androgen induced arousal of aggressive behaviorin adulthood. Female mice were ovariectomized at age 30 days and either administered testosterone propionate daily for 20 days or a control injection of oil for 20 days. Forty five days after the termination of the pretreatment, all mice were given testosterone propionate and tested in pairs for fighting. Following androgen administration in adulthood 75% of the pairs pretreated with testosterone propionate in immaturity fought, but only 25% of the pairs of females pretreated with oil in immaturity fought. It was concluded that the potential for androgen administered in infancy to induce masculinization of female mice with respect to androgen aroused aggressive behavior in adulthood exists for at least one month after birth. 8 references. (author abstract)

081264 Hoyland, Valerie J.; Shillito, Elizabeth E.; Vogt, Marthe. Agricultural Research Council Institute of Animal Physiology, Babraham, Cambridge, England The effect of parachlorophenylalanine on the behaviour of cats. ***British Journal of Pharmacology (London).*** **40:659-667, 1970.**

The effect of parachlorophenylalanine on the behavior of cats was investigated. Male and female kittens and adult cats were given p-chlorophenylalanine orally. After treatment, some of the male cats showed mounting behavior and the kittens and nonestrous females showed an increase in treading and rubbing which was similar to one aspect of proestrus behavior. The treated animals also appeared to suffer from skin irritation and showed increased restlessness which accompanied sleep deprivation. Injection of 5-hydroxytryptophan (5-HTP) stopped abnormal sexual activity and restored normal sleep for about 5 hours. The temporary restoration of normal behavior by 5-HTP supports the view that the depletion of 5-HTP by p-chlorophenylalanine was the cause of the behavioral changes. Thus cerebral 5-HTP appears to act as an inhibitor of sexual behavior in cats and has this role in males and, to some extent, in females. 15 references. (Author abstract modified)

06 METHODS DEVELOPMENT

079973 Supprian, Ulrich. Psychiatrische Universitatsklinik, Martinistrasse 52, Eppendorf, 2000 Hamburg 20, Germany /A technique to demonstrate the effect of a psychopharmaceutical drug in a psychopathological longitudinal section by numeric and graphic means./ Technik zur Darstellung eines Psychopharmaka-Effektes im psychopathologischen Langsschnitt mit numerischen und graphischen Mitteln. ***Arzneimittel-Forschung (Aulendorf).*** **20(7):963-967, 1970.**

A technique is reported on how to demonstrate graphically the psychopathological course of endogenous depressions, making the effect of a psychopharmaceutical drug obvious. The raw data obtained with the aid of a phenomenon - near item list and a self-rating scale are transformed, interpolating a weighting matrix so that the psychopathological central dimensions of the endogenous depression (which are operationally defined by this matrix) are isolated. These values are graphically represented by a group of lines. The interpretation makes use of the daily differences and is put in relation to the total degree of severity and a normsyndrome. The evidencing capacity of the technique is demonstrated by means of some illustrations from a clinical study on 3-chloro-5-(3-dimethylamino -propyl)-10,11-dihydro-5H-dibenzo (b,f) azepine hydrochloride (Anafranil). 18 references. (author abstract)

080631 Kaul, Pushkar N.; Conway, Michael W.; Clark, Mervin L.; Huffine, James. College of Pharmacy and Experimental Therapeutics Unit, University of Oklahoma, Norman, Oklahoma 73069

Chlorpromazine metabolism I: quantitative fluorometric method for 11 chlorpromazine metabolites. ***Journal of Pharmaceutical Sciences.*** **59(12):1745-1749, 1970.**

Eleven chlorpromazine metabolites have been reacted with dimethylaminonaphthyl sulfonyl chloride to obtain fluorescent products. The reaction has been standardized and adapted to quantitative determination of nanogram amounts of the metabolities. A procedure for application to biological fluids has been developed. Addition and recovery experiments on urine and plasma indicate that the method is applicable to the study of the pharmacokinetic aspects of chlorpromazine metabolites in human subjects. 13 references. (Author abstract)

081261 Delbarre, B.; Dumas, G.; Guionniere, M. Laboratoires Pfizer-Clin B.P. 42, F-37 Amboise, France An automated open field method. ***Psychopharmacologia (Berlin).*** **18(2):227-230, 1970.**

A new automated apparatus for recording movement and rearing of rats in the open field method has been produced using electronic techniques. This equipment permits the evaluation of depressant and excitatory actions of drugs on the central nervous system. Having observed that the rat always supported itself against the walls of the chamber on rearing, automatic recording of this activity was developed.

07 EARLY CLINICAL DRUG TRIALS

075878 Brandsma, Maynard. Leisure World Medical Center, Laguna Hills, California 92653 Preliminary experience with medazepam (Nobrium) in the management of psychophysiologic reactions. *Psychosomatics.* 11(3):197-22, 1970.

Preliminary experience with medazepam (Nobrium) is described for the management of psychiatric, or functional somatic disorders in which anxiety-tension was a characteristic symptom. The daily dosage ranged from 10 to 60mg in divided doses. Duration of treatment ranged from 3 days to 17 weeks. The results were favorable in 49 patients, in 14 of whom symptoms completely disappeared. Side effects, mainly drowsiness, occurred in 10 patients. Laboratory data (17 patients) showed no abnormalities which could be attributed to medazepam. Statistical analysis showed highly significant improvement (p less than 0.001) due to medazepam in the major anxiety symptoms, 'average improvement score' and overall clinical status. Further controlled investigation of medazepam is recommended, particularlyin patients with psychiatric and psychophysiologic conditions in which anxiety and tension predominate. 4 references. (Author abstract modified)

078931 Benady, D. R. Child Guidance Clinic, The Shirehall, Shrewsbury, Shropshire, England Cyproheptadine hydrochloride (Periactin) and anorexia nervosa: a case report. *British Journal of Psychiatry (London).* 117(541):681-682, 1970.

Cyproheptadine hydrochloride (Periactin) was used as an adjunct to treatment in a classical case of anorexia nervosa in a 12-year-old-girl. While the drug had been shown to be a potent antihistamine and to have powerful appetite stimulating properties, its use had not been reported in a case such as the present one. Details of the case are presented for a nearly 3 year period. As an adjunct to psychotherapy, cyproheptadine hydrochloride appeared to be useful in helping a patient with anorexia nervosa to gain weight, and it is inferred that the drug would be helpful in other, similar cases. Side effects were not apparent in this case. 4 references.

079146 Vencovsky, E. Psychiatricka klinika KU, Plzen, Czechoslovakia /New psychopharmaceuticals for clinical practice./ Nova psychofarmaka pro klinickou praxi. *Ceskoslovenska Psychiatrie (Praha).* 66(6):326-330, 1970.

It appears that further progress in the field of new neuroleptics would follow a trend toward production of tablets with delayed action for peroral use, or of depot neuroleptics with prolonged action for parenteral administration. In this field, 2 new psychoactive drugs deserve attention, namely: 1) ORAP 24, generic name --pimozide, produced by Janssen in Beerse; and 2) IMAP 7, generic name -- fluspirilene, Janssen. There is also a neuroleptic -- Defectone, generically carpipramine, produced by Yoshitomi, Osaka. The present experience permits the conclusion that all 3 neuroleptics represent an important therapeutic contribution to treatment of schizophrenic and nonschizophrenic psychotic processes. Pimozide and fluspirilene deserve top attention for their therapeutic effectiveness in psychiatric clinical use. 4 references. (Journal abstract modified)

079863 Henry, P.; Dayne, D.; Bergouignan, M. Laboratoire Cassenne, France /Clinical tests of a new, prolonged-action neuroleptic agent, Pimozide./ Essai therapeutique d'un nouveau neuroleptique a action prolongee, le Pimozide. *Annales Medico-Psychologiques (Paris).* 1(3):611-616, 1970.

The findings of clinically testing the new, prolonged action neuroleptic agent, Pimozide are reported. The tests were conducted with 30 patients over an 18 month period. A unique value of the drug lies in the fact that it can be administered at any time of day. The secondary effects are moderate; the extrapyramidal effects are especially rare and of small importance. Eighty percent of the patients benefited from the drug, 60% of these in a very marked fashion. Its antideliriant and hallucinolytic powers place Pimozide in the ranks of the major neuroleptic agents. In view of its high tolerance, it appears especially useful in neuroleptic cures of long duration. 5 references.

079969 Berzewski, H.; Hippius, H.; Petri, H.; Schiffter, R. Psychiatrische Klinik II der Freien Universitat, Nussbaumallee 36, 1000 Berlin 19, Germany /Clinical study on a new piperidyl-phenothiazine derivative (A 124)./ Klinische Untersuchungen mit einem neuen Piperidyl-phenothiazin-Derivat (A 124). *Arzneimittel-Forschung (Aulendorf).* 20(7):949-952, 1970.

2-Acetyl-10-(3-(4-methoxypiperidyl)-propyl)-phenothiazine (A 124) as a piperidyl derivative of phenothiazine is closely related in its chemical structure to 3-methylthio-10-(2-(1-methyl-2-piperidyl)-ethyl) -phenothiazine (thioridazine) and 10-(3-(4-hydroxypiperidino) -propyl)-phenothiazine-carbonitrile (propericiazine). Clinical study revealed a sedative and sleep promoting effect of A 124. The fast and favorable influence on disorders of sleeping - waking rhythm is more pronounced in A 124 than it is in thioridazine and propericiazine. The sedative effect is about the same as that of thioridazine. After extended application, about the 20th day of therapy, psychotic symptoms in the fields of perception and thinking are influenced favorably. Propericiazine influences these symptoms more quickly and intensively at daily doses of 150mg but the frequency of extrapyramidal motor side-effects is far greater at these dosages. Similar to thioridazine, A 124 exerts a slightly antidepressive activity. The most improtant side-effects of A 124 are disturbances of the autonomic system. The liver function should be examined regularly because changes of the serum enzymes GOT and GPT have been observed. The symptoms of extrapyramidal system are of minor consequence. The mild neuroleptic effect and the rarely occurring side-effects of slight intensity make A 124 suited for long-term therapy of psychoses. 11 references. (author abstract modified)

079971 Geisler, L.; Rost, H.-D. Medizinischen Kliniken und Polikliniken der Justus-Liebig-Universitat, Fiedrichstrasse 27, 63 Giessen, Germany /Studies in man on the influence of a new psychopharmaceutical drug, 1-((methylamino)-dibenzo(b,e,)bicyclo-(2,2,2)octadiene-hydro ochloride, on the CO2 sensitive central respiratory regulation./ Untersuchungen am Menschen uber den Einfluss des neuen Psychopharmakons 1-((Methylamino)methyl)-dibenzo(b,e)bicyclo-(2,2,2)octadien- -hydrochlorid auf die CO2-sensible zentrale Atemregulation. *Arzneimittel-Forschung (Aulendorf).* 20(7):957-958, 1970.

In 30 subjects with normal respiratory conditions, 1-((9methylamino)methyl)-dibenzo(b,e)bicyclo-(2,2,2)octadiene - hydrochloride (benzoctamine, Tacitin) was tested for its influence on the CO2 sensitive central respiratory regulation in the back respiration test. Further, in 10 patients with chronic obstructive lung diseases, the arterial blood gases were measured several times after i.v. injection of the compound. The results of both test series show that benzoctamine given as a psychopharmaceutical drug stimulates respiration in man. 17 references. (author abstract)

079986 Angst, J.; Cornu, F.; Heimann, H.; Poldinger, W.; Steiner, H. Forschungsabteilung der Psychiatrischen Universitatsklinik Zurich, Lenggstrasse 31, CH-8008 Zurich, Switzerland /2-Chloro-11(4'-methylpiperazino)-dibenzo-(b,f)(1,4)-oxazepi ine), (Sum 3170), a new neuroleptic substance: Results of an interclinical study./ 2-Chlor-11(4'-methylpiperazino)-dibenzo-(b,f)(1,4)-oxazepin (Sum 3170), ein neues Neurolepticum: Ergebnisse einer interklinischen Prufung. *Arzneimittel-Forschung (Aulendorf).* 20(7):967-970, 1970.

At 4 Swiss university clinics, a derivative of the antidepressive substance dibenzepine, 2-chloro-11(4'-methylpiperazino)-dibenzo-(b,f) (1,4)-oxazepine (Sum 3170), has been tested with regard to its sedating and antipsychotic action in 99 cases of psychotic agitation of different etiology. The substance has proven to be a highly potent neuroleptic with marked sedative, motility inhibiting and antipsychotic action. Its sedative effect is approximately comparable to that of levomepromazine or clopenthixol, and its antipsychotic effect to that of clopenthixol. In addition, it induces a marked inhibition of motility which is favorable in feeble minded patients with motor excitation or in Huntington's chorea cases. The substance is moderately tolerated; there are frequent extrapyramidal side-effects, which, however, can be controlled by early application of antiparkinson drugs. The substance is especially effective in acute agitated or productive schizophrenic syndromes, and in mania. Its handling requires a certain amount of experience. 1 reference. (author abstract)

080031 Gannon, P.; Itil, T.; Keskiner, A.; Hsu, B. Missouri Institute of Psychiatry, University of Missouri School of Medicine, 5400 Arsenal Street, St. Louis, Missouri 63139 Clinical and quantitative electroencephalographical effects of MK 940. *Arzneimittel-Forschung (Aulendord).* 20(7):971-974, 1970.

Clinical and EEG studies were performed on trans-10,11-dihydro-5,10-epoxy-5-(3-(methylamino)propyl)-5H-dibenzo (a,d)cyclohepten-11-ol hydrogen maleate (MK 940) a compound which exhibits pharmacological properties resembling those of tricyclic an-

tidepressive substances. The clinical symptoms influenced were conceptual disorganization and to some extent influence on depression. The EEG demonstrated no changes characteristic for antidepressive substances. MK 940 caused alterations more like those of a centrally stimulating drug. The clinically effective dose, devoid of side-effects, ranges between 8 and 24mg/day. 5 references. (author abstract)

080098 van Krevelen, D. Arn.; Maresca, A.; Schreurs-Dijkstra, M. Scheveningseweg 3,'s-Gravenhage, The Netherlands Evaluation of Tegretol in the treatment of behaviour disorders in children: methodology and results. ***Acta Paedopsychiatrica (Basel).*** **37(7-8):222-234, 1970.**

The therapeutical effect of Tegretol in children with severe behavior disorders was evaluated relevant to brain pathology without clinical neurological symptoms. Seven Dutch and 7 Italian nonepileptic hospitalized children from 6 to 19 years were treated with Tegretol, the effect of which was studied during 8 weeks. The methodology with regard to the use of questionnaires is discussed and the influence of emotional attitudes of personnel and staff is shown (antidrug v. placebo attitude). The outcome is evaluated by means of analysis of observation reports, EEG curves and Bourdon test results. The favorable effect of Tegretol is manifested in a notable decrease of aggressiveness and hypermotility, whereas slight side effects were only temporary. Disparities between the Dutch and the Italian dataconcerning the influence of the drug upon EEG disorders, may probably be explained by the fact that in the Italian institution gross cerebral damage plays a more important role in the etiology of the pathological behavior than in the Dutch psychotherapeutic center. 9 references. (Author abstract modified)

08 DRUG TRIALS IN SCHIZOPHRENIA

075872 Hollister, Leo E. Veterans' Administration Hospital, 3801 Miranda Avenue, Palo Alto, California 94304 Choice of antipsychotic drugs. ***American Journal of Psychiatry.*** **127(2):186-190, 1970.**

Antipsychotic drugs are the most useful treatment available for the most serious psychiatric disorders. Despite the plethora of available, a rational choice of few will provide a full range of therapeutic effects. Drugs must be chosen in relation to the special needs of individual patients. Some special considerations in choosing a drug or drugs are: 1) the patient's past experience, 2) the side-effects to the patient, 3) whether short- or long-term treatment is necessary, and 4) the severity of the psychosis. 15 references. (Author abstract modified)

075879 Abuzzahab, Faruk S., Sr. Departments of Psychiatry and Pharmacology, University of Minnesota Medical School, University of Minnesota, Minneapolis, Minnesota Some uses of haloperidol in the treatment of psychiatric conditions. ***Psychosomatics.*** **11(3):188-193, 1970.**

Haloperidol has been evaluated as to effectiveness in the treatment of a variety of psychiatric conditions by an open investigation conducted on 41 variously diagnosed psychiatric patients, the majority of whom were schizophrenic, but 3 individuals with Huntington's Chorea and 4 suffering from Gilles de la Tourette syndrome were also included. Ten patients were dropped from the study prior to the completion of 4 weeks of treatment. Of the 31 patients who completed the study, 3 showed marked improvement, 19 moderate improvement, 5 slight improvement and 4 no change. Extrapyramidal side effects appeared in 24 patients and with the exception of 4 cases were adequately controlled by the concurrent administration of antiparkinsonian medication. Haloperidol, found to be a rapid acting and nontoxic agent, was felt to be valuable in the treatment of a wide variety of psychiatric problems. 4 references. (Author abstract modified)

075881 van Praag, H. M.; Breetveld, J.; van Mesdag-Etty, H.; Westerhuis, R.; Pen, A.; Schut, T. Department of Biological Psychiatry, Psychiatric Clinic, State University, Groningen, The Netherlands A controlled comparative study of fluphenazine and fluphenazine enanthate in acute and chronic psychotic patients. ***Psychiatria, Neurologia, Neurochirurgia (Amsterdam).*** **73(3):165-175, 1970.**

A long acting neuroleptic should meet the requirement of being equal in therapeutic potency to the corresponding compound without protracted action. In a controlled comparative study, depot fluphenazine (Anatensol enanthate) proved to meet this requirement, both in acute psychotic and in chronic psychotic patients. Depot fluphenazine frequently (more frequently

than the mother substance) gives rise to extrapyramidal side effects, especially during the first few days following injection. These can be adequately controlled with antiparkinson drugs (and prevented if sufficiently large doses of these drugs are used). Advantages, disadvantages, indications and contraindications of neuroleptic depot therapy are discussed. 20 references. (Author abstract)

075944 Hoffer, A. 800 Spading Crescent East, Saskatoon, Saskatchewan, Canada Childhood schizophrenia: a case treated with nicotinic acid and nicotinamide. *Schizophrenia.* 2(1):43-53, 1970.

A case of childhood schizophrenia treated with nicotinic acid and nicotinamide is described. The biochemical treatment was successful over a 12 year period in overcoming the metabolic disorder of a child originally labeled retarded. 38 references.

076003 Goldberg, Harold L.; DiMascio, Alberto, Chaudhary, Basudeo. West Ros Park Mental Health Center, Boston State Hospital, Boston, Massachusetts A clinical evaluation of prolixin enanthate. *Psychosomatics.* 11(3):173-177, 1970.

Prolixin enanthate appears to be significantly superior to oral phenothiazine in drug reluctant patient. It was observed that it was most outstanding in paranoid individuals. It was remarkably useful in patients seen in the home who refused oral medication and many of whom would have requiredhospitalization had this drug not been available. The drug was easily administered intramuscularly in the deltoid region by a nurse making home visits and was well tolerated by all of the home treated patients. Since completion of the study, it hasbeen successfully employed in after care with the cooperation of the Visiting Nurses Association.

078932 Morris, P. A.; MacKenzie, D. H.; Masheter, H. C. Kinsway Hospital, Derby, DE3, 3LZ, England A comparative double blind trial or pimozide and fluphenazine in chronic schizophrenia. *British Journal of Psychiatry (London).* 117(541):683-684, 1970.

The relative efficacy of pimozide and fluphenazine in the treatment of chronic schizophrenia is tested in a double-blind trial involving 30 patients. The effects of once daily pimozide (9mg) and fluphenazine (15mg) were found to be similar. Parkinsonian symptoms were less marked in degree and frequency in the patients taking pimozide. Laboratory investigations showed no changes outside the normal range. 3 references. (Author abstract modified)

079993 Vojtechovsky, M. Vladislava Vancury 15, Prague 5-Smichov, Czechoslovakia /Influence of centrophenoxin on memory disturbance after electroshock./ Beeinflussung der Gedachtnisstorungen nach Elektroschock mit Centrophenoxin. *Arzneimittel-Forschung (Aulendorf).* 20(7):882-884, 1970.

A protective effect of p-chlorophenoxyacetic acid 2-dimethylaminoethyl ester (Centrophenoxin, Lucidril) with regard to experimentally provoked disturbances of memory was tested. Twelve patients with chronic schizophrenia received 6 electroshocks (ECT) each and were subsequently given 4 tests (Wechsler Memory Scale, Benton Test, learning of 6 paired associations and word experiment according to Kent - Rosanoff with 30 verbal stimuli). Centrophenoxin (750mg/day orally, 6 patients) and placebo (16 patients) was given during the ECT period and during the 30 days following it. Another group of schizophrenic patients who received placebo without ECT were tested at the same time as the other patients (2, 15 and 29 days after last ECT). There was no significant difference in memory disturbances after ECT between the centrophenoxin group and the placebo group. Centrophenoxin medication had an unexpected favorable effect onassociation content in the Kent -Rosanoff word association test. A transient improvement (lasting 2 weeks) in the content of associations after ECT up to normal values could be demonstrated. 7 references. (author abstract)

080143 Dogliani, P.; Senini, G.; Bertuzzi, F. Ospedale Psichiatrico Provinciale, Piazzale delle Cerociate 2, 29 100 Piacenza, Italy Clinical observations on the therapeutic activity of flupentixol in the treatment of chronic schizophrenia. *Arzneimittel-Forschung (Aulendorf).* 20(8):1126-1140, 1970.

(author abstract) 9-(3-(4-(2-Hydroxyethyl)-piperazin-1-yl)-propylidene)-2-trifluoro-methlthioxanthene(flupentixol), being a neuroleptic drug in the series of thioxanthene compounds, was used in clinical trials involving a total of 67 patients (34 males and 33 females) suffering from chronic schizophrenia. All these patients had been previously treated with chlorpromazine in dosages between 200 and 400mg daily. Flupentixol was ad-

ministered p.o. in daily dosages of 2 to 6mg (mean 5.4mg) to 22 male patients for periods of 47 to 100 days (mean 91), and in daily dosages of 2 to 5mg (mean 3.3) to 25 female patients for periods of 21 to 90 days (mean 82). In 21 of these patients responding favorably to the drug, treatment was continued for an average 201 days at an average daily dosage of 4.78mg. In another group of schizophrenic patients, flupentixol was administered at an average daily dosage of 11mg for 3 months. Therapeutic results at the end of 3 months of treatment were adjudged good in 49 percent of the cases, with a definite gain over the results previously obtained with chlorpromazine; in 40 percent there were no appreciable differences of effectiveness between chlorpromazine and the test drug. Long-term treatment in selected patients produced favorable results in 90.5percent of the cases. Flupentixol proved effective not only in regard to 'active' symptoms of schizophrenia (hallucination, delusion), but especially in regard to the 'passive' symptoms. The tolerability of flupentixol was generally good, also in patients receiving high dosages of the drug. Side-effects were reported in about 34 percent of the cases, with a predominance of parkinsonian manifestations. 19 references. (author abstract modified)

080355 Varsamis, J. Department of Psychiatry, Faculty of Medicine, University of Manitoba, Winnipeg 3, Manitoba, Canada Antipsychotic drugs: an essential tool of community psychiatry. ***Canadian Journal of Public Health (Toronto).*** **61(5):432-435. 1970.**

The place of antipsychotic tools as an essential tool of community psychiatry in care of schizophrenic patients is reviewed and evaluated. The effectiveness of antipsychotic drugs in the treatment of schizophrenia has been established beyond a reasonable doubt. Their introduction facilitated the successful application of the concepts of community psychiatry. With drug therapy acutely ill schizophrenics improve sufficiently over a relatively short period of time to be discharged to the community. Consequently, the care of many schizophrenics has been transferred from the mental hospital to the community. The limitations of drug therapy are summarized as follows: a) maintenance doses have to be taken for long periods. As in all chronic illnesses a sizeable proportion of patients do not take drugs as prescribed, failure to take medication is followed by relapse and eventual rehospitalization; b) a few patients are resistant to drug therapy and a considerable number have already deteriorated irreversibly by the time they come to medical attention; c) two complications of long term phenothiazine treatment have been recently described: an irreversible extrapyramidal syndrome and a skin eye syndrome. 16 references. (Author abstract modified)

080506 Tanimukai, H.; Ginther, R.; Spaide, J.; Bueno, J. R.; Himwich, H. E. Department of Psychiatry and Neurology, Osaka University Medical School, Osaka, Japan Detection of psychotomimetic N,N-dimethylated indoleamines in the urine of four schizophrenic patients. ***British Journal of Psychiatry (London).*** **117(539):421-430, 1970.**

In order to check the hypothetical suggestion that under loading conditions the formation of various N,N-dimethylated indoleamines might be facilitated in the body, which might mediate the psychotic effect of methionine with a MAO inhibitor on schizophrenic patients, the body fluids of 4 schizophrenic patients were checked for psychotomimetic amines. In addition to tryptamine and serotonin bufotenin (5-hydroxy-N, N-dimethyltryptamine) was found both in free and conjugated forms in the urine of the patients under dietary control when they were receiving tranylcypromine, with or without cysteine loading. The amount of bufotenin was estimated to be as little as 4-10mg/day per 24 hr. urine; one-half in the free, one-half in the conjugated form. In the absence of monoamine oxidase blockade bufotenin was also excreted in some patients, but less than 1 mg/day. Increases of urinary bufotenin and other N-methylated indoleamines were observed about two weeks before the mental and behavioral symptoms of the schizophrenic patients worsened, and these elevated levels continued during the period of behavioral exacerbations. 24 references. (Author abstract modified)

080609 Fisher, Gary. University of California, Los Angeles, California The psycholytic treatment of a childhood schizophrenic girl. ***International Journal of Social Psychiatry (London).*** **16(2):112-130, 1970.**

A report is given of one of 12 autistic and schizophrenic children who were experimentally treated with lysergic acid diethylamide (LSD) and psilocybin in a research study which began in early 1962 and terminated in the middle of 1963.

Some judments were made as to what these experiences were about. The hypothesis used in the research and treatment program involving 12 children diagnosed as childhood schizophrenics is that psychosis is a massive defensive system of repression avoidance denial in the service of protecting the individual from experiencing his feelings. The rationale behind the use of psychedelic agents with psychotic children was that these drugs have the capacity to activate or chemically energize various areas of the brain to an extreme degree resulting in vivid experiencing in the area of perception, emotion, memory and feeling. Experiences and feelings ordinarily denied awareness receive proportionately more energy causing them to break into a state of consciousness which is less strongly dominated by the usual defenses and values which one has developed. Without the usual complicated defensive structures and censures, the individual is able to reexperience himself in a far less distorted way and to reevaluate the worthiness of his essential self. 8 references.

09 DRUG TRIALS IN AFFECTIVE DISORDERS

075867 Shull, Willie K.; Sapira, Joseph D. St. Vincent's Hospital and Medical Center of New York, 153 West 11th Street, New York, New York 10011 Critique of studies of lithium salts in the treatment of mania. ***American Journal of Psychiatry.*** **127(2):218-222, 1970.**

All available studies of lithium therapy of mania (comprising 805 patients) have been reviewed to determine whether lithium's pharmacologic efficacy has been demonstrated in the customary manner. All studies reviewed except for 1 were found to have serious methodological deficiencies. It is concluded that the available data demonstrate neither efficacy nor inefficacy, primarily because of inadequate experimental design. 41 references. (Journal abstract modified)

078542 Murphy, Dennis L. Laboratory of Clinical Science, National Institute of Mental Health, Bethesda, Maryland 20014 L-DOPA, behavioral activation and psychopathology (Unpublished paper). Bethesda, Maryland, NIMH, 1971. 17 p.

L-DOPA is well known as a precursor of the neurotransmitters dopamine and norepinephrine and has recently become well known for its therapeutic effects in Parkinson's disease. DOPA is also a psychoactive agent with profound behavioral effects in some individuals but minimaleffects in others. DOPA administration to animals produces marked increases in brain dopamine, much smaller and variable changes in norepinephrine, as well as some other less studied neurochemical changes. While the localization of dopamine to the striatum, globus pallidus and substantia nigra in brain has long suggested its importance in motor function, the possible role of dopamine in behavior and mood, particularly in man, has been less certain. Some quantitative measurements of the psychoactive effects of DOPA in man are discussed. Changes in rated behavior, sleep and learning in a group of depressed patients treated with large oral doses of L-DOPA are considered. These effects of DOPA will be examined from the perspectives of the psychological changes observed in other patient groups receiving DOPA, the effects of DOPA on animal behavior and on amines and amine metabolites, and a theory implicating excessive psychomotor activation in the genesis of maladaptive behavior. 103 references. (Author abstract)

078732 Booij, Joh. Amsterdam, The Netherlands Treatment of depressions according to 'target symptoms.' ***Psychiatria, Neurologia, Neurochirurgia (Amsterdam).*** **73(6):419-425, 1970.**

A discussion is presented regarding the efficacy of treating psychiatric target symptoms of depression by various methods, including psychopharmacology, rather than attempting to cure the illness producing the emotional disorder. It appears that an antiquated approach toward the treatment of depression is still being used, with emphasis on controlling anxiety and agitation while the cause of the psychic disturbance is being overlooked. Special attention must be paid to the various types of depressive illness and the metabolic and biochemical changes which often are involved. For these reasons, caution is suggested in the treatment of target symptoms of psychically disturbed patients and it is urged that more effort be directed toward discovering the fundamental causes of the psychoses. 26 references.

081038 Bunney, William E., Jr.; Murphy, Dennis L.; Brodie, H. Keith H.; Goodwin, Frederick K. Section of Psychiatry, Laboratory of Clinical Science, National Institute of Mental Health, Bethesda, Md. 20014 L-Dopa in depressed patients. ***Lancet (London).*** **No. 7642:352, 1970.**

L-dopa was given to 10 depressed patients who were not suffering from Parkinson's disease to assess its direct effect on mood. One patient responded to L-dopa administration, but an increase in psychotic features has also been observed. In all data collected, only 2 depressed patients responded favorably to L-dopa, while 4 showed no reaction and 4 showed an increase in the psychotic elements of their illness. The possibility of a difference between the metabolic effect of L-dopa in parkinsonism and in depression is suggested. Substantial increase in the levels of cerebrospinal fluid homovanillic acid are found in the depressed patients treated with L-dopa. A biphasic effect of L-dopa has been observed in animals depending on the dose administered. 13 references.

081152 Melia, P. I. St. Patrick's Hospital, Dublin, Ireland Prophylactic lithium in recurrent affective disorders: a four year study. *Journal of the Irish Medical Association (Dublin).* 63(400):353-357, 1970.

Twenty nine patients who suffered from frequently recurrent affective disorders were studied. The majority of patients were bipolar manic-depressives. No patient satisfying the criteria for selection was excluded. An open evaluation of lithium's prophylactic action in 18 patients, who remained in the trial for a 3 to 4 year period, showed than in 10 it had an apparent marked effect; in a further 2 it was relatively effective; and in 6 it was ineffective. A comparison of patients who apparently responded to lithium with those who did not, showed that responders had shorter histories of affective disorder, had higher pre-lithium episode frequencies and were more likely to have a diagnosis of bipolar manic-depressive disorder than that of any other diagnostic subgroup. The reasons why 11 of the 29 patients dropped out of the trial are given. Five patients stopped taking lithium and consequently acted as controls with respect to the natural history of the illness. One of these had a spontaneous remission; 4 continued to have frequent episodes; and 1 died, probably from suicide. There was 1 case of goiter arising during lithium therapy (the patient remained euthyroid) and 1 case of serious toxicity with rapid and complete recovery. 21 references. (author abstract modified)

081516 Cavanagh, R. J. Naval Hospital, National Naval Medical Center, Bethesda, Maryland 20014 The treatment of manic-related diseases with lithium carbonate. *Military Medicine.* 135(3):199-202, 1970.

Twelve of 14 patients demonstrated improvement or remission of the manic-like state of their illness from 2 to 12 days after institution of treatment with lithium carbonate by the Department of Neuropsychiatry at the National Naval Medical Center in Bethesda, Maryland. Each patient, after complete physical and neurological examination, was placed on an initial dose of at least 600mg lithium carbonate daily. Maintenance doses ranged between 600mg and 1200mg daily. Those who were maintained on lithium did not experience a recurrence of a stateof excitability although long-term followup is not available. The results are suggestive of the therapeutic efficacy of lithium salts in the management of the manic aspects of psychiatric disorders. This review of treatment covers a 19 month period. Case histories are described for each of the 14 patients. Long-term followup of the current study is essential in helping to clarify the effects of many variables, for example, other medications. As this study was not controlled, it is impossible to conclude that the use of lithium was the responsible agent in every case. Major and minor tranquilizers and psychotropic agents had been used with these patients. 14 references.

10 DRUG TRIALS IN NEUROSES

075868 Rickels, Karl; Gordon, Paul E.; Weise, Charles C.; Bazilian, Stanford E.; Feldman, Harold S.; Wilson, Daniel A. 203 Piersol Building, University Hospital, 3400 Spruce Street, Philadelphia, Pennsylvania 19104 Amitriptyline and trimipramine in neurotic depressed outpatients: a collaborative study. *American Journal of Psychiatry.* 127(2):208-218, 1970.

In a controlled double-blind clinical trial, conducted in depressed neurotic outpatients, comparing trimipramine, amitriptyline and placebo as to their respective antidepressant properties, 122 patients from 4 populations were the subjects. Amitriptyline produced the most and placebo the least amount of symptomatic improvement, with trimipramine slightly less efficacious than amitriptyline; general practice patients tended to improve the most and medical clinic patients the least. It is suggested that amitriptyline may be more potent than trimipramine at equal dosages, as evidenced by its greater production of side effects, and that

the small difference in clinical efficacy between the 2 drugs may thus be dosage related. 13 references. (Journal abstract modified)

075871 Prange, Arthur J., Jr.; Wilson, Ian C.; Knox, Angeline; McClane, Thomas K.; Lipton, Morris A. University of North Carolina School of Medicine, Chapel Hill, North Carolina 27514 Enhancement of imipramine by thyroid stimulating hormone;clinical and theoretical implications. *American Journal of Psychiatry.* 127(2); 191-199, 1970.

Thyroid stimulating hormone (TSH), when combined with imipramine, produces a more rapid recovery from depression than does imipramine alone. It seems more potent than triiodothyronine in potentiating imipramine, but dose differences prevent accurate comparison. This hormone has the clinical disadvantage of being long acting and difficult to control. Depressed patients show thyroid indices within the normal range. Serum indices of thyroid state respond normally to TSH injection, but ankle reflex time is not accelerated. Tantalizing clues have appeared, but the mechanism by which thyroid hormones potentiate tricyclic antidepressants remains unknown. 41 references. (Author abstract)

076292 Rickels, Karl; Howard, Kay; Covi, Lino; Park, Lee C.; Lipman, Ronald S.; Uhlenhuth, Eberhard H. 203 Piersol Building, University Hospital, 3400 Spruce Street, Philadelphia, Pennsylvania 19104 Differential reliability in rating psychopathology and global improvement. *Journal of Clinical Psychology.* 26(3):320-323, 1970.

Correlations between observer and doctor ratings of psychopathology (8 point scale) and global improvement (7-point scale) from 2 psychiatric drug studies are reported. The reliability of psychopathology ratings was found to be low, but the ratings of global improvement were quite reliable. It was suggested that global neurotic psychopathology is a relatively diffuse concept, and therefore difficult to assess reliably. In rating global improvement, however, the patient's initial appearance serves as a clinical criterion. Furthermore, the patient frequently verbalizes how improved he feels, thus providing more structure, which leads to greater agreement between raters in rating global improvement. 7 references. (Author abstract)

076347 Simeon, Jovan; Fuchs, Maria; Nikolovski, Oliver; Bucci, Luigi. Department of Psychiatry, New York Medical College, 5 East 102nd Street, New York, New York 10029 Ketipramine in the therapy of depression in outpatients. *Psychosomatics.* 11(4):342-346, 1970.

There is need for antidepressant drug therapies with a more rapid onset than imipramine or amitriptyline and an efficacy higher than the 60% usually reported with their use. In early clinical trials in Europe, ketipramine was found to be as effective as imipramine, with fewer secondary effects. As part of the evaluation of new treatments in patients who had not improved with standard regimens, a double-blind study with ketipramine was undertaken in a community mental health clinic. In an outpatient depressive population ketipramine was as effective an antidepressant as imipramine, with equivalent dose range, and with slightly lesser degrees of secondary effects. 2 references. (Author abstract modified)

078212 Kits, T. P.; van Praag, H. M. Department of Biological Psychiatry, Psychiatric University Clinic, Oostersingel 59, Groningen, The Netherlands A controlled study of the antidepressant effect of p-chloro-N-methylamphetamine, a compound with a selective effect on the central 5-hydroxytryptamine metabolism. *Acta Psychiatric Scandinavica (Kobenhavn).* 46(4):365-373, 1970.

A controlled study is made of the antidepressant effect of p-chloro-N-methylamphetamine (CMA), a compound with selective effect on the metabolism of 5-hydroxytryptamine (5-HT) in the central nervous system. CMA produces a distinct decrease in the cerebral concentrations of 5-HT and 5-hydroxyindoleacetic aic (5-HIAA) in various test animals in which it exerts no significant influence on the catecholamine concentrations. The influence of CMA on the central monoamine metabolism, therefore, is the opposite of that of the mother substance: methamphetamine (Methedrine; Pervitin). In view of the selective effect of MCA on the 5-HT metabolism the question arose as to whether (and if so, how) CMA influences affectivity. In a previous pilot study it was established that CMA has an antidepressant effect on depressive patients. The study is repeated under controlled conditions with 50 recently hospitalized patients admitted in connection with a depressive syndrome. The double blind study in which 3 x 30mg CMA or an equivalent number of identical placebo tablets

were administered, confirmed the antidepressant effect on depressive patients obtained in the pilot study: the CMA group proved to be superior to the placebo group at a level of significance of 5%. No significant side effects were observed. A possible explanation of the antidepressant effect of CMA is speculatively discussed. 19 references. (Author abstract modified)

079967 Hohnbaum, M.; Sattes, H. Universitats-Nervenklinik, Fuchsleinstrasse 15, 87 Wurzburg, Germany /Clinical treatment of depressive syndromes with noxiptilin./ Klinische Behandlung depressiver Syndrome mit Noxiptilin. *Arzneimittel-Forschung (Aulendorf).* 20(7):940-943, 1970.

Sixty one women suffering from depressions were treated with 5-(2-dimethylamino-ethoxy-imino)-5H-dibenzo(a,d)cyclohepta-1,4-diene hydrochloride (Noxiptilin, Agedal), for 6 months. Noxiptilin is suited very well for the treatment of inhibited endogenous and inhibited psychogenous depressive conditions. The success varied in the treatment of hypochondric and delusionary depressions. In 4 patients with agitated depressions, only moderate improvement was obtained. The drug must be dosed individually. During the first 3 to 5 days the daily dose was below the maintenance dose calculated later. The daily applied maintenance dose of the different collectives ranged from 143.7to 216.0mg. The physical side-effects of Noxiptilin were not appreciable. Undesired side-effects of psychic character were 2 cases of maniac post fluctuations and 5 instances of delirious symptoms, which readily regressed after stopping the drug. All of the patients showing drug induced delirium were older; a deficient blood circulation in the brain could not be excluded in all cases. 10 references. (author abstract modified)

081121 Tapia, Hector Lara; Grajales, Armando. Servicio de Psiquiatria, Instituto Nacional de Neurologia (S.S.A.) Insurgentes Sur 3877, Mexico 22, D. F. /Clinical considerations on the treatment of depression with chlorimipramine./ Consideraciones clinicas sobre el tratamiento de la depresion con clorimipramina. *Neurologia-Neurocirugia-Psiquiatria (Mexico City).* 11(2):159-167, 1970.

The results of research with a new major antidepressant, chlorimipramine are presented. The new drug constitutes an important step forward in the treatment of various mild, severe, acute and chronic depressive states for its rapidity and depth of action, the span and duration of its effects and its special tolerance. This very favorable impression is the result of a study made on 111 patients that have been observed over the last 12 months. Its superiority over other drugs of the same type lies in the rapid and powerful action which permits emergency treatment in severe depressive conditions and for its good tolerance. It can, therefore be very helpful to those patients whose conditions forbid the use of seismotherapy. 25 references. (author abstract)

11 DRUG TRIALS IN MISCELLANEOUS DIAGNOSTIC GROUPS

075942 Kellner, Robert. Department of Psychiatry, University of New Mexico School of Medicine, Albuquerque, New Mexico 87106 Drugs, diagnoses, and outcome of drug trials with neurotic patients: a survey. *Journal of Nervous and Mental Disease.* 151(2):85-96, 1970.

Published double-blind drug trials with neurotic patients are surveyed. Trials with depressed neurotic patients were carried out with monoamine oxidase inhibitors, and tricyclic drugs, and a few trials were carried out with amphetamine derivatives or amphetamines in combination with other drugs. Drug trials with neurotic patients in other diagnostic categories were also carried out with barbiturates, tranquilizers, the benzodiazepines, diphenylmethane derivatives. The results are tabulated according to the drugs used and according to the diagnostic categories of the patients, and the findings are discussed. 102 references. (Journal abstract)

076233 Faretra, Gloria; Dooher, Lillian; Dowling, Jean. Queens Children's Psychiatric Hospital, 80-45 Winchester Boulevard, Queens Village, New York 11427 Comparison of haloperidol and fluphenazine in disturbed children. *American Journal of Psychiatry.* 126(11):1670-1673, 1970.

The new major tranquilizer, haloperidol, was compared with fluphenazine in the treatment of disturbed children, most of them schizophrenic. While the overall effectiveness of the 2 drugs was similar, haloperidol appeared more effective in reducing provocativeness and autism; it also seemed to act more quickly. Side effects were mainly extrapyramidal and were easily controlled with biperiden. On the basis of the study, it appears that haloperidol is an effective antipsychotic agent in the treatment of disturbed children. 6 references. (Author abstract modified)

079215 Moffatt, W. R.; Siddiqui, A. R.; MacKay, D. N. Eastern Special Care Management Committee, Muckamore Abbey Hospital, Co., Antrim, Northern Ireland The use of sulthiame with disturbed mentally subnormal patients. *British Journal of Psychiatry (London).* 117(541):673-678, 1970.

A double-blind, crossover trial of sulthiame as a tranquilizer rather than as an anticonvulsant is described. Forty two severely subnormal, hospitalized patients with marked and apparently intractable behavior abnormalities took part. Detailed assessments of behavioral changes were made, with the use of rating scales, by nursing observers. The findings were as follows: 1) Sulthiame was significantly effective in reducing the incidence of disturbed behavior. 2) There was insufficient evidence to suggest that it affected the variety of disturbed behavior. 3) Most of the patients had taken part in a earlier trial with pericyazine and chlorpromazine and had shown no improvement; this suggests that sulthiame may well be effective in cases where other tranquilizers have failed. 4) The so called placebo effect did not materialize. 5) There were no observable side effects during the trial. 6) The addition of sulthiame to standard anticonvulsant therapy brought about a decrease in seizure frequency in only 1 of 25 epileptic patients. 9 references. (Author abstract modified)

079288 Ey, Henri; Bohard, Francois. Hopital Psychiatrique, 28 Bonneval, France /Therapeutic medication in chronic delerium: combination of prochlorperzine (Tementil) and levomepromazine (Nozinan). Resultats d'une therapeutique medicamenteuse dans les delires chroniques: association de la prochlorperazine (Tementil) et de la levomepromazine (Nozinan). *Evolution Psychiatrique (Paris).* 35(1):251-295, 1970.

Reported individually are 100 observations of the use of therapeutic medication in cases of chronic delerium. The study reveals that the use of the combination prochlorperazine levomepromazine (Tementil-Nozinan) does not, in general, produce dramatic results in neurotic states and with acute, deleriant psychoses. It does not seem superior to other therapeutic agents with cases of schizophrenic psychosis. On the other hand, it appears to be the medication of choice in cases of paranoic psychosis (21 successes in 47 cases), improving considerably the prognosis for this psychosis.

079746 Tapia, Hector Lara. Instituto Nacional de Neurologia, S.S.A. Insurgentes Sur No. 3877, Mexico 22, D. F., Mexico /Clinical considerations about the treatment of various acute psychotic states with thiotixene./ Consideraciones clinicas sobre el tratamiento de diversos estados psicoticos agudos con thiotixene. *Neurologia-Neurocirugia-Psiquiatria (Mexico).* 11(3):225-233, 1970.

Sixty one patients comprising 11 categories of psychoses were included in this study, and were treated with a new thioxanthene derivate, thiotixene. Very low doses were used with excellent results; the best improvements were obtained in an average of 5 weeks. Once again, this drug has demonstrated to be a powerful antipsychotic with moderate and controllable extrapyramidal side effects. The best results were obtained in acute psychotics or in patients with acute treatment. These results were obtained also in paranoid forms of psychoses. The modifications of the liver functions tests are moderate and reversible by decreasing dosage or by discontinuing the drug. 23 references. (Journal abstract)

079858 Bastie, Y. S.R.E. de Premontre 02, France /Suppressing withdrawal convulsions by Depakine in alcoholic detoxification cures./ Suppression des crises d'epilepsie du sevrage par le Depakine dans les cures de desintoxication ethylique. *Annales Medico-Psychologiques (Paris).* 2(3):400-404, 1970.

Results reported are from clinical tests in which Depakine was used to suppress the epileptic withdrawal seizures sometimes present in cures by alcoholic detoxification. Favorable results were obtained from the systematic use of Depakine during 1 year with more than 500 alcoholics. The general atmosphere of the withdrawal situation is considerably eased by the freedom from the frightening impact of convulsive manifestations. To the numerous indications for Depakine which already exist, this new use is added. There exists a real, natural affinity between the drug and the ailment which it treats, namely, that of alcoholic epilepsy and, more specifically, the epileptic crises of withdrawal. 16 references.

079859 Bornstein, S.; Kannas, S.; de Rivieres, H. Sere; Bureau, D.; Postel, J. Hopital de Maison-Blanche, 3, avenue J.-Jaures, 94-Neuilly-sur-Marne, France /Therapeutic interest in Hydrosarpan-711 in depressive states and in the psychiatric pathology of gerontological states./ Interet

therapeutique de l' Hydrosarpan 711 dans les etats depressifs et la pathologie psychiatrique du presenium. ***Annales Medico-Psychologiques (Paris).*** **2(3):433-444, 1970.**

Findings reported are from a clinical test of Hydrosarpan-711 in conditions of chronic, cerebral, and circulatory insufficiency attendant on the approach of senility. The evidence is favorable. Perfectly tolerated, the administration of the drug could be extended to depressive, melancholic, or psychotic states where vascular factors were critical. The use of Hydrosarpan-711 was found satisfactory in treating postshock syndromes. With ambulatory patients, it is in the area of the presenile depressions that Hydrosarpan-711 finds one of its better curative, and perhaps preventive, indications. 3 references.

079864 Boutillier, H. author address not given /Clinical tests of a new anxiolytic, medazepam (Nobrium)./ Essais cliniques d'un nouvel anxiolytique, le Medazepam (Nobrium). ***Annales Medico-Psychologiques (Paris).*** **1(3):617-630, 1970.**

A report on clinical tests of a new anxiolytic, medazepam (Nobrium), a derivative of the benzodizepines is presented. The tests were conducted with 70 female patients of a psychiatric hospital. The product appeared efficacious; 50 satisfactory results were observed as opposed to 20 failures, the latter occuring with cases where Nobrium was not used for its specific action on anxiety but to test its possible sedative properties. In general, tolerance is good and effects on biological constants most commonly explored are practically negligible. At equal dosage, Nobrium produces an effect much like that of Valium, along with sedative and myorelaxant subeffects. The good tolerance permits augmentation of dosage without complication and the drug appears to be especially well adapted for the treatment of patients prior to their return to ambulatory care.

079912 Eddy, T. P. Department of Human Nutrition, London School of Hygiene and Tropical Medicine, London, England Advances in nutrition and dietetics. ***Practitioner (London).*** **205(1228):527-534, 1970.**

Among important causes of ill health are diseases associated with nutrition, such as protein and calorie malnutrition, disaccharidase deficiency and milk intolerance, deficiencies of vitamin B12 and folic acid, and chronic and subclinical vitamin deficiency. Other relevant aspects include the interrelationship of nutrition and infection, rickets and osteomalacia, and the effects of diets high in saturated fatty acids or sugar in ischemic heart disease. Improvement and complete cure of severe confusional dementia was obtained in 2 elderly patients treated with folic acid for B12 - resistant megaloblastic anemia. Psychiatric syndromes and dementia caused by deficiencies of vitamin B12 which could occur with normal peripheral blood flow and normal appearances on marrow biopsy have been reported. Megaloblastic anemia was reported in 13 percent of women who received only iron in pregnancy, and there is considerable evidence of folate deficiency in deprived old people and alcoholics. Knowledge of nutrition is advancing rapidly, moving into the realms of cellular and molecular biology. Most malnutrition is caused by ignorance and it is primarily a social disease, often starting in early childhood when habits are formed, and rooted in the culture of those whom it afflicts. 59 references.

079963 Lutzenkirchen, Hans; Mertens, Hans Georg. Neurologische Universitatsklinik, Luitpoldkrankenhaus, 87 Wurzburg, Germany /The treatment of chronic pain syndromes: Analgetic effect of aneuroleptic substance./ Behandlung chronischer Schmerzsyndrome: Analgetischer Effekt eines Neurolepticums. ***Arzneimittel-Forschung (Aulendorf).*** **20(7):930-931, 1970.**

In order to isolate the analgetic effect of a potent neuroleptic drug, 124 patients with chronic neurological pain syndrome weretreated with benperidol. It was found that a certain type of pain to be characterized as diffuse, fluctuating, burning, undefined, is particularly susceptible to this medication. With regard to the clinical picture, the best results were observed in phantom syndromes and amputation syndromes, diabetic polyneuropathy and chronic trigeminal neuralgia of the anesthesia dolorosa type. In radicular neuralgia, acute trigeminal neuralgia and pain due to nerve infiltrations, the results were not satisfactory. In such cases, highly potent thymoleptic substances may be very effective. Potent neuroleptic and thymoleptic drugs have an analgesic effect which is not tied to a sedative hypnotic action. There are indications for a syndrome specific pain therapy with psychotropic drugs. 6 references. (author abstract)

079974 Celesia, Gastone G.; Barr, Arlene N. Department of Neurology, 1954 East Washington

Avenue, Madison, Wisconsin 53704 Effectiveness and limitations of long-term levodopa therapy in parkinsonism. ***Wisconsin Medical Journal.*** **69(10):227-230, 1970.**

Forty five patients with Parkinson's disease were treated with levodopa for 5 to 14 months. Twenty nine patients improved and 16 did not. Adverse reactions were frequent but reversible. The major limiting factors of the therapy were the emergence of dyskinesia and psychiatric disturbances. In spite of the frequency of side-effects, levodopa is an effective agent in the treatment of parkinsonism. Patients with postencephalitic parkinsonism and pretreatment dementia tended to tolerate levodopa less well than other parkinsonian patients and developed side-effects at lower doses. 8 references. (author abstract)

079994 Bauer, A.; Mosler, A. Neurologisch-Psychiatrischen Klinik des Stadtischen Krankenhauses, Gotenstrasse 6-9, 623 Frankfurt/M.-Hochst, Germany /Treatment of delusion of parasitosis./ Die behandlung des dermatozoenwahnes. ***Arzneimittel-Forschung (Aulendorf).*** **20(7):884-886, 1970.**

The syndrome of the delusion of parasitosis has been observed in an already advanced case of presenile dementia, in a case of beginning cerebral arteriosclerotic dementia with depressive symptoms, and in 2 additional cases of otherwise physically and mentally healthy patients who showed pathological pneumoencephalographic findings. Of these 4 cases 3 could be treated. In the second case fluphenazine was not effective, but under Limbatril, the depressive as well as the tactile hallucinatory syndromes disappeared. Fluphenazine was effective, however, in the 2 cases of internal and external hydrocephalus without clinical manifestation who presented the tactile hallucinatory delusion in almost pure form. The effect did not persist after medication was stopped. Continued medication, however, caused the symptoms to disappear completely. The prompt drug dependent effect of this potent substance acting on the brainstem is an empirical finding which may be included into considerations regarding syndrome genesis. 16 references. (author abstract)

080041 Guth, E.; Wruhs, O. RZ Meidling, 37 Kundratstrasse, A-1120 Vienna XII, Austria /Proposals for improving the treatment of brain damaged patients./ Vorschlage zur Besserung des Schicksales Hirnverletzter. ***Wiener Medizinische Wochenschrift (Wien).*** **120(36):597-601, 1970.**

Improvement in the treatment of severe brain damage is discussed. For the treatment of vegetative damage, the use of ganglion blocking agents is recommended. Because it must be a long term treatment, chlorpromazine is not suitable for this purpose, being toxic under these conditions; however, dixyrazine (Esucos) is effective. A lytic mixture which is recommended consists of the proper proportions of Esucos, Hydergin and Phenergan. The psychomotor restlessness, however, is not responsive to this mixtuure, which should be reserved only for vegetative damage. An infusion of Hemineurin in an 0.8percent solution is recommended for relieving restlessness, since this drug does not affect circulation, but acts as a muscle relaxant and relieves psychic tension. Rapid changes can occur in these patients, and the medication may have to be administered more often than was originally prescribed. It is therefore necessary for the physician to see the patient frequently in order to control the medication, and the nurses must be specially trained to recognize changes in these patients. 21 references.

080142 Cocito, E.; Ambrosini, G.; Arata, A.; Bevilacqua, P.; Tortora, E. Ospedale Psichiatrico Provinciale di Genova-Quarto, Via Redipuglia 95, 16 100 Genova, Italy Clinical evaluation in 112 psychiatric patients of a butyrophenone neuroleptic, dehydrobenzperidol (R 4749). ***Arzneimittel-Forschung (Aulendorf).*** **20(8):1119-1125, 1970.**

Dehydrobenzperidol or Droperidol (1-(1-(3-(p-fluorobenzoyl)-propyl)-1,2,3,6-tetrahydro-4-pyridyl)-2- benzimidazolinone, R 4749) being a neuroleptic in the group of butyrophenones, was used in clinical trials involving a total of 112 hospitalized male patients (mean age: 37 years old); of these, 104 were suffering from schizophrenia, and 8 from atypical depressive syndromes. The average duration of disease was 5 years. The daily dosage of the test drug varied from 1 to 19mg (average 8mg). Therapeutic results were excellent in 52 percent of the patients, good in 32 percent, fair in 8.9percent and poor or nil in 6.3percent. Extrapyramidal side-effects, usually of the hyperkinetic type (tasikinesia, akathisia) were observed in 16 percent of the cases. In further clinical experiments, the effects of dehydrobenzperidol were compared with those in 45 hospitalized patients with schizophrenia, predominantly

of the paranoid variety. This was a double-blind controlled trial, in which 22 patients were treated with dehydrobenzperidol and 23 were treated with haloperidol: the 2 groups were assembled randomly. Both drugs were given in gradually increasing doses, starting with 0.6mg daily and reaching 14.5mg in some cases; the average dose was 6.32mg daily for dehydrobenzperidol and 6.0mg for haloperidol; the average duration of treatment was 74 days for dehydrobenzperidol and 51 days for haloperidol. Therapeutic results were assessed by applying the Rating Scale for Quantification of Psychotic Symptom Severity of Wells Goodrich. The effects of the 2 drugs were compared at 30 days of administration in 40 cases (average daily doses: dehydrobenzperidol 5.79mg, haloperidol 5.75mg), and at 60 days in 12 cases. At the end of treatment, favorable results were recorded in 90 percent of the patients treated with dehydrobenzperidol and in 78 percent of those treated with haloperidol. In the comparisons made at 30 and 60 days of treatment, the rate of favorable results was 83 percent for dehydrobenzperidol and 75 percent for haloperidol. 22 references. (author abstract modified)

080563 Teichmann, H.; Knaape, H. H. Universitats-Nervenklinik Rostock, Abteilung fur Kinder-Neuro-Psychiatrie, Rostock, Germany /Testing the performance under aponeuron of otherwise normal school children with a tetendency toward reduced drive and easy tiring./ Die Leistungen antriebsgeminderter, leicht ermudbarer Normalschulkinder unter Aponeuron im Arbeitsversuch. *Psychiatrie, Neurologie und Medizinische Psychologie (Leipzig).* 22(8):298-304, 1970.

Using a Pauli performance test, the effects of aponeuron were studied in 20 normal school children between 10 and 16 years of age who showed a tendency toward reduced drive and easy tiring. Results were: 1) with a daily dosage of 20mg in the morning and 10mg at noon, the pure drug increases the mental capacity by increasing by 12.6% the number of sums worked out per unit of time in the Pauli test; 2) the placebo effect associated with the drug was determined to be 22.2% so that there was a total increase in capacity under trial conditions of 34.8%; and 3) the improvement of mental capability is thought to be a genuine one, since quantitative increases in performance were not accompanied by more nervous working methods, reduction in the quality of work, or greater fatigue at the end of the 60 minute test period. 15 references. (Author abstract modified)

080635 Grant, Richard H. E.; Stores, Olga P. R. David Lewis Colony, Alderley Edge, Cheshire, England Folic acid in folate-deficient patients with epilepsy. *British Medical Journal (London).* 4(5736):644-648, 1970.

A controlled clinical trial is made to assess effects of folic acid treatment on incidence of seizures, behavioral aspects, personality and a number of cognitive functions in folate deficient epileptics. A double-blind trial using folic acid 15 mg. daily and identical placebo was carried out in 51 epileptic patients having a serum folate level below 3.6ng./ml. Treatment was for a minimum of 6 months and in 41 patients was for more than 1 year. There were no significant changes in the frequency of seizures, behavior, and personality, or in a number of cognitive functions. 18 references. (Author abstract modified)

081039 Meier, Manfred J.; Martin, William E. University of Minnesota Medical School, Minneapolis, Minnesota Measurement of behavioural changes in patients on L-dopa. *Lancet (London).* No. 7642:352-353, 1970.

An attempt was made to quantify changes in the intrinsic properties of patterned motion cycles in 54 patients on L-dopa therapy for Parkinson's disease. Performance was assessed using a pegboard of 25 holes into which the patient had to place 25 pegs, alternating hands, in 5 minutes. The substantial differences between the performance levels of the incapacitated and impaired subgroups when they were on their previous medication were considerably narrowed after L-dopa, and this improvement applied to both hands. The results suggest that the previous medications were selectively beneficial to the impaired group. Although markedly improved, both groups differ significantly from the retested normal controls. The use of these and other quantitative studies may yield precise operational criteria for determining the limits of behavioral change in L-dopa therapy. 2 references.

081144 Seebandt, G. 4032 Lintorf, Am Eichforstchen 72, Germany /Experience with propericiazin (Aolept) in the treatment of children with disturbed psychomotor functions and restlessness./ Erfahrungen mit Propericiazin in der Behandlung kindlicher psychomotorischer Funktions-

storungen und Unruhezustande. Arzneimittel-Forschung (Aulendorf). 20(7):937-939, 1970.

An account of the effective treatment of children with psychomotor and functional disturbances by means of the neuroleptic phenothiazine derivative, propericiazin or Aolept (10-(3-(4-hydroxypiperidino) -propyl)-phenothiazine-2-carbonitril), is presented. The patient population comprised boys of the aged of 6 to 16 years, living in a home for feebleminded children, and were characterized under 2 degrees of imbecility or idiocy. The improvement was evaluated under the headings: exacerbation, unchanged, and successful therapy. This improvement was further evaluated in the areas of psychomotor performance, social adaptability, and the degree of interest and involvement in play activities. The results are tabulated under the headings: premature birth and multiple birth, age, hereditary deficit, exogenous cerebral damage, cerebral seizures, degree of mental deficiency, dosage, duration of therapy, effect of therapy, and side -effects. The results indicated that Aolept is a particularly effective medication for children of the type described here and that its tolerance is within acceptable limits. 5 references.

081298 Lieberman, Abraham N.; Caviness, Verne S., Jr.; Shattuck, Calvin L. Department of Pharmacology, New York University Medical Center, 550 First Avenue, New York, New York 10016 Metrazol and the evaluation of seizures. ***Military Medicine.*** **135(3):194-198, 1970.**

A major responsibility of the Neurology Service of the United States Air Force Hospital, Tachikawa, Japan, is the evaluation of patients who have spontaneously lost consciousness to determine whether or not it was an epileptic attack. A group of 43 patients with a history of focal or generalized seizures and 25 patients without seizures were tested to determine the reproducibility of seizures by the injection of metrazol. At or below 5mg of metrazol per kg of body weight, 79% of epileptics and only 20% of nonepileptics had positive responses. Metrazol activation is meaningful only if the patient's symptoms, including the seizure, are reproduced. 17 references.

12 PSYCHOTOMIMETIC EVALUATION STUDIES

075859 Weingartner, Herbert; Snyder, Solomon H.; Faillace, Louis A.; Markley, Herbert. Department of Psychiatry and the Behavioral Sciences, The Johns Hopkins University, Baltimore, Maryland Altered free associations: some cognitive effects of DOET (2,5-dimethoxy-4-ethylamphetamine). ***Behavioral Science.*** **15(4):297-303, 1970.**

Normal adult males were administered DOET (2,5-dimethoxy-4-ethylamphetamine) and d-amphetamine, at 2 separate times in a double-blind experimental design. DOET in low doses (1.5mg/70kg) produced no gross behavioral or perceptual changes. DOET did alter Ss free associations at the time of maximal drug uptake. Ss produced lower frequency, less common, free associations with DOET. Although the associations Ss produced with DOET occur less frequently in association norms they were neither bizarre or idiosyncratic responses. In addition, these free associations were at least as reproducible as the associations produced under no drug or amphetamine conditions. This new psychotropic agent, in low doses, appears to be particularly effective in altering normal cognition without producing disorganizationin thinking or perception. 11 references. (Author abstract)

076254 Barron, Stanley P.; Lowinger, Paul; Ebner, Eugene. Community Psychiatric Consultants, Scarborough, Ontario, Canada A clinical examination of chronic LSD use in the community. ***Comprehensive Psychiatry.*** **11(1):69-79, 1970.**

A report on chronic lysergic acid diethylamide (LSD) users is detailed, with emphasis on the long-term effects on behavior and mental function in those who have not had a psychiatric illness related to LSD. The subjects were 20 paid volunteers who had taken LSD an average of 38 times over a period of from 6 months to 5 years, and were utilizing LSD with decreasing frequency. Long standing personality disorders are very frequent among chronic LSD users, but it must be noted that in every case these disorders antedated the use of the drug and did not appear to be worse in 2 to 3 years of LSD use. Subjects' claims of personal benefits could not be substantiated, and the study indicates that while the group showed no evidence of increasing personal or social disorganization, no significant benefit from LSD use was noted. 18 references.

079956 Lienert, G. A. Psychologisches Institut der Universitat, 4 Dusseldorf, Germany /Configuration frequency analysis of some LSD effects./ Konfigurationsfrequenzanalyse einiger Lysergsaurediathylamid-Wirkungen. *Arzneimittel-Forschung (Aulendorf).* 20(7):912-913, 1970.

Four operationally defined alternative symptoms obtained from 65 subjects in the initial phase of LSD action have been studied with regard to syndrome formation by means of configuration frequency analysis. Four syndromes have been found. Three of them are monosymptomatic: transient 'blacking out'; transient thought disruption; and transient or repeated discharge of affect. One is a tetrasymptomatic syndrome, comprising the 3 symptoms mentioned above plus hallucinatory phenomena. The attempt to identify similar syndromes by means of factor analysis has not been successful, as the 4 symptoms did not yield correlation coefficients (Phi) differing from zero. A configuration frequency analysis carried out without the symptom 'black out' gave the same result as the one done with all 4 symptoms. 8 references. (author abstract)

13 MECHANISM OF ACTION: PHYSIOLOGICAL, BIOCHEMICAL AND PHARMACOLOGICAL

075968 Huffer, Virginia; Levin, Leon; Aronson, Harriet. Psychiatric Institute, University of Maryland School of Medicine, Baltimore, Maryland 21201 Oral contraceptives: depression and frigidity. *Journal of Nervous and Mental Disease.* 151(1):35-41, 1970.

An attempt was made to correlate use of oral contraceptives with the development of mood and/or sexual disturbances and, if a relationship were found, to determine whether such disturbance fell into any predictable pattern. Hypotheses were chosen in 7 broad categories: 1) previous history of psychiatric disorders; 2) current life stresses; 3) attitudes toward contraception; 4) symptoms due to expectations of the effect of the pill; 5) marital and sexual adjustment; 6) physiological alteration secondary to pill usage; 7) reaction to pregnancies. The affected women could not be differentiated from their controls by means of any of the hypothesized variables. However, 2 factors tended to correspond with the development of adverse reaction: 1) use of the combined (as opposed to sequential) type of contraceptive pill and 2) age of the subject. The results suggest that women who have adverse reactions to oral contraceptives might represent a biochemically different subgroup in whom estrogen progesterone steroids are thetriggering mechanisms for mood and sexual disturbances. 21 references. (Author abstract modified)

076016 Diamond, A. Leonard; Cole, Robert E. University of Hawaii, Honolulu, Hawaii 96822 Visual threshold as a function of test area and caffeine administration. *Psychonomic Science.* 20(2):109-111, 1970.

The threshold luminance of a small circle was studied as a function of its area (varied from 2.69 min to 26.87min in radius) and for different dosages of caffeine (0, 1.5, and 3 grains). The zero caffeine condition shows the classical decrease in threshold with increased area. With caffeine administration, the slope of this threshold area function remains unchanged, although the entire function shifts downward (threshold decreases equally for all areas) increasingly with an increasing amount of caffeine. The results combined with previous caffeine experiments suggest a theoretical interpretation that caffeine causes the 'on' visual pathways to become more sensitive to light. 15 references. (Author abstract)

078213 de Jonghe, F. E. R. E. R.; van der Helm, H. J. Akademisch Ziekenhuis, Bij de Universiteit van Amsterdam, Amsterdam-Oud west, Eerste Helmersstraat 104, Amsterdam, The Netherlands Plasma concentrations of thioridazine in patients with depression: a preliminary report. *Acta Psychiatrica Scandinavica (Kobenhavn).* 46(4):360-364, 1970.

A study is made of plasma concentrations of thioridazine in patients with depression because large individual differences in blood levels of patients treated with certain psychoactive drugs have been shown to exist. An attempt is made, to determine whether the levels of thioridazine correlate with therapeutic effects. Plasma concentrations in 57 patients treated with thioridazine were determined. Earlier results of Mellinger et al. were corroborated. Large individual variations in the plasma levels in patients receiving the same dosage were found. The plasma concentrations were higher in the failure group than in the success group. The possibility that plasma determinations of this drug could be of help in establishing a rational therapy is discussed. 7 references. (Author abstract modified)

078555 Pinelli, Paolo. Istituto di Clinica Malattie Nervose e Mentali, Universita Cattolica del S. Cuore, Rome, Italy /Considerations on the hyperkinesia of L-Dopa: significant biochemical and anatomical deficiencies./ Considerazioni sulle ipercinesie da L Dopa: significato del deficit biochimico e del deficit anatomico. *Archivio di Psicologia Neurologia e Psichiatria (Milan).* 31(5):405-416, 1970.

The results of electromyographic investigation in patients with Parkinsonism treated with L-Dopa are discussed, and the evaluation of the literature on this subject suggests the following conclusions: a) Akinetic - hypertonic syndrome is derived from a functional disturbance in the operating or neuronal assemblies (or schemas) which assure the motor automatic patterns. These are realized in the normal brain partly by overcoming, partly by imposing on primary postural automatisms. b) Hereditary and acquired schemas are located in hierarchical different levels of the Central nervous system. They are formed by: 1) a central pool of neurons which are excited mainly with reflex mechanisms; 2) an integrative fringe modulating the preceding pool through; 3) a dopaminergic inhibitory system. c) A fall in the level of dopamine enhances the activity of the central pool as a consequence rigidity together with akinesia are promoted. d) A cellular impoverishment, particularly at the level of the inhibitory system, hinders the modulation of the central pool even if a substitutive therapy with dopamine is effected. 33 references. (Journal abstract)

078733 Biemond, A. Neurological Department, Wilhelmina Gasthuis, Amsterdam, The Netherlands On Binswanger's subcortical arteriosclerotic encephalopathy and the possibility of its clinical recognition. *Psychiatria, Neurologia, Neurochirurgia (Amsterdam).* 73(6):413-417, 1970.

Two cases of Binswanger's subcortical arteriosclerotic encephalopathy are described, both confirmed by autopsy. An attempt is made to delineate 6 clinical points in favor of this diagnosis. The significance of vasodilator treatment as an aid in the diagnosis of Binswanger's disease is demonstrated in a third case, a clinical observation not confirmed anatomically. 6 references. (Author abstract modified)

079139 Pogady, J.; Hudakova, G.; Cerven, J.; Muncnerova, L. Krajska psychiatricka liecebna v Pezinku, Czechoslovakia /Dynamic control of acid-base equilibrium during some forms of shock therapy./ Dynamicke sledovanie priebehu acidobazy pri niektorych sokovych liecbach. *Ceskoslovenska Psychiatrie (Praha).* 66(6):321-325, 1970.

Dynamic control of acid base balance during 4 forms of shock therapy was investigated by Astrup's micromethod. The patients received insulin, pentylentetrazole, Cardiazole, carbon dioxide, and electroshock treatments. The acid base level was determined before treatment, during the comatous state, immediately after the shock and 30 and 60 minutes thereafter. Among the data obtained were: hydrogen ion concentration, partial pressure of CO2, base equivalents, active bicarbonate, basic reserve, partial pressure of O2, and saturation. It was found that insulin produces hypoxia of the brain and a resultant shift in internal milieu giving rise to slight alkalosis. This finding contradicts present reports in the literature. Cardiazole and electroshock result in statistically significant acidosis. Acidosis after Cardiazole is more severe than after electroshock. In both cases, acidosis probably results from muscular reaction to the treatment. Carbon dioxide coma produces exogenous acidosis which could be termed an acidotic coma, whereas the coma produced by electroshock of Cardiazole is of central origin. 7 references. (Journal abstract modified)

079965 Matussek, N.; Benkert, O.; Schneider, K.; Otten, H.; Pohlmeier, H. Max-Planck-Institut fur Psychiatrie, Kraepelinstrasse 2, 8 Munich 23, Germany /Effect of a decarboxylase-inhibitor (Ro 4-4602), combined with L-dopa, on retarded depressive patients./ Wirkung eines Decarboxylasehemmers (Ro 4-4602) in Kombination mit L-dopa auf gehemmte Depressionen. *Arzneimittel-Forschung (Aulendorf).* 20(7):934-935, 1970.

The effect of N1-(D2-seryl-N2-(2,3,4-trihydroxybenzyl) -hydrazine)-HC1) plus DOPA on 36 cases of endogenous retarded depression has been studied in a double-blind experiment. With 5 patients of the medication group, the medication had to be discontinued because of nausea and vomiting. In 31 patients (medication group: 18; placebo group: 13), the time course over 11-18 days could be studied by means of a self-rating scale and by the registration of blood pressure, heart frequency, respiration of blood pressure, heart frequency, respiration and psychogalvanic skin reflex. The rating scales showed a slight improvement of the depression in 67 percent (12) of cases in the medication group, as compared to 30 percent (5)

cases of the placebo group. Four patients in the medication group and 6 patients in the placebo group became worse. In each group, there were 2 patients who showed no change. There was a tendency towards improvement of retarded depression under medication with this combination of substances. The physiological reactions did not show any difference between medication group and placebo group. The improvement in patients of both groups could not be correlated with any of the physiological measures obtained. 23 references. (author abstract)

079966 Poldinger, W.; Gehring, A.; Sutter, W. Psychiatrische Universitatsklinik, Wilhelm-Klein-Strasse 27, 4000 Basel, Switzerland /Accelerated action of psychotropic drugs effected by pyrithioxin./ Die Beschleunigung des Wirkungseintrittes von Psychopharmaka durch Pyrithioxin. *Arzneimittel-Forschung (Aulendorf).* 20(7):936-937, 1970.

In addition to a standardized intramuscular application of chlorprothixen, 20 depressive patients received pyrithioxin or placebo orally in a double-blind study. Changes in symptoms during the first 10 days of treatment were rated with a standardized method. There was a significant difference between the 2 groups on the second and third days of medication: the pyrithioxin group showed an earlier improvement of certain symptoms than the placebo group. These results demonstrate that the action of chlorprothixen sets in earlier when pyrithioxin is applied simultaneously. 4 references. (author abstract)

081143 Fischbach, R. Landesnervenklinik, Neurologische Abteilung, A-5020 Salzburg, Austria /Intragastric telemetric measuring of pH during thymoleptic medication./ Intragastrale telemetrische pH-Messungen bei thymoleptischer Behandlung. *Arzneimittel-Forschung (Aulendorf).* 20(7):923-925, 1970.

Reference is made to previous experiments where it was shown that treatment with thymoleptics causes a loss of acidity in the gastric juice, both free and total acidity. In addition, there is a decrease in absorption of the thymoleptics of the imipramine category, which can only be restored by acid substitution. In order to investigate this matter further, tests were carried out in a group of 24 patients whose gastric juice was examined by a duodenal probe, 13 of which revealed normal acid values and 11, below normal to anacid values, subsequent to thymoleptic therapy. These results were not considered unequivocal due to the method of inserting the probe. A further study in 16 patients was conducted by means of an endogastric capsule known as the 'Heidelberg capsule', which is a telemetric method of measuringacidity. The thymoleptic agents administered to these patients (with depression) were: amitryptiline, Ro 4-6011, imipramine, dimethacrine, desipramine or chlorimipramine, at dose levels comparable to those in prior experiments. In 9 patients, a pH value of 3.0to 6.0was observed, the rest showing normal or hyperacid values, thus confirming previous experiments. 6 references.

14 MECHANISM OF ACTION: BEHAVIORAL

075860 Bloch, H. Spencer. Judge Baker Guidance Center, The Children's Hospital Medical Center, Boston, Massachusetts Brief sleep treatment with chlorpromazine. *Comprehensive Psychiatry.* 11(4):346-355, 1970.

A technique utilizing brief periods of sound narcosis induced by chlorpromazine is described. It proved to be an effective and efficient therapeutic - diagnostic -management tool for severely behaviorally disturbed and uncontrolled patients in an open crisis oriented mileu ward in Vietnam where no other facilities for managing such patients existed. The patient's behavioral state rather than a nosological diagnostic category constituted the indication for a trial of brief sleep treatment. The success of the treatment could usually be predicted from the promptness with which the patient succumbed to the soporific effects of chlorpromazine upon its initial administration and from the 'soundness' of his sleep. Thus it became particularly helpful in differentially diagnosing acute or transient psychotic stress states from the more entrenched, persistent ones. The degree to which this therapeutic tool may have aborted more lasting psychotic reactions was not assessed through the use of control patients, nor was the possible efficacy of drugs other than the antipsychotic, chlorpromazine, determined. No hypothesis for the possible specific therapeutic effects of chlorpromazine induced sleep is advanced, though some appear in the world literature. A description of this technique and a discussion of its results are presented because of the potential implications of this relatively simple and safe technique for the crisis management of severely disturbed psychiatric patients, especially in settings which

have limited psychiatric treatment resources. 29 references. (Author abstract modified)

075873 McNair, Douglas M.; Fisher, Seymour; Sussman, Carol; Droppleman, Leo F.; Kahn, Richard J. Psychopharmacology Laboratory, Division of Psychiatry, Boston University School of Medicine, Boston, Massachusetts Persistence of a drug-personality interaction in psychiatric outpatients. *Journal of Psychiatric Research (Oxford).* 7(4):299-305, 1970.

This followup study reevaluates 4 small groups of psychiatric outpatients who, 4 months earlier, had completed a double-blind trial of diazepam. A drug -personality interaction demonstrated during the 2 week trial was that high acquiescer - placebo and low acquiescer - diazepam groups improved significantly more than the high acquiescer - diazepam and low acquiescer - placebo groups. The followup data supported 2 principal conclusions about the long range combined effects of medication and personality: They can modify patients' reactions to subsequent treatment; they also can endure for a considerable period. Thus the same 2 groups who improved most during the clinical trial significantly less often prematurely quit their subsequent therapy, and further, they maintained their significantly greater symptomatic improvement 4 months later. As a whole, the followup sample reported significant additional improvement after the drug trial. The patients, their posttrial therapists and an independent social worker considered both the medication and other aspects of participation in the drug trial to have benefited subsequent therapy. Another finding was that high acquiescers, reinforcing previous doubts that high acquiescers are conformers. Some potential biasing and confounding influences upon the results are discussed, and the need is stressed for replication and for further studies of the mechanism of the drug personality interaction. 9 references. (Author abstract)

075884 Bordeleau, J. M.; Charland, P.; Tetreault, L. Department of Research, St. Jean-de-Dieu Hospital, Montreal, Canada Hypnotic properties of nitrazepam (Mogadon) (a comparative study of chlordiazepoxide, diazepam, nitrazepam, secobarbital and placebo in psychiatric patients). *Diseases of the Nervous System.* 31(5):318-323, 1970.

This comparative study of chlodiazepoxide 50mg, diazepam 10mg, secobarbital 200mg, nitrazepam (mogadon) 10mg and of placebo aims at proving the hypnotic properties of these benzodiazepines. Nitrazepam, like secobarbital, reduces the duration of sleep induction and increases the duration of sleep. Chlordiazepoxide and diazepam do not differ significantly from placebo by their action on these 2 parameters of sleep. Side effects were mild in all cases and the medications were well tolerated although at 50mg. chlordiazepoxide has given more side effects than placebo. 9 references. (Author abstract modified)

076276 Finlayson, Paul; Burnheim, Ronald B.; Boots, Una J. North Ryde Psychiatric Centre, Dept. of Public Health, Sydney, New South Wales, Australia A comparison of Propanidid (Epontol) and Thiopentone anaesthesia in ECT. *British Journal of Psychiatry (London).* 116:79-83, 1970.

0A comparative drug trial was conducted in a routine electrconvulsive treatment (ECT) program on 20 psychiatric inpatients between the 2 anesthetic agents propanidid and thiopentone sodium. The former showed a significantly faster rate of physical arousal and recovery of mental functions, as well as a lower incidence of the conspicuous confusional state which is specific to the immediate post-ECT recovery period. 8 references. (Author abstract)

078223 Michael, Carmen M.; Kantor, Herman I.; Shore, Herbert. Department of Psychiatry, University of Texas (Southwestern) Medical School at Dallas, Dallas, Texas 75235 Further psychometric evaluation of older women - the effect of estrogen administration. *Journal of Gerontology.* 25(4);337-341, 1970.

The research investigated whether administration of estrogen to older post-menopausal women would result in improved psychological and behavioral adaptation or at least in a slower rate of psychological decline. The results showed that there were significant Hospital Adjustment Scale differences between estrogen and placebo Ss. It appears that the administration of estrogen to this population may result in some improvement in adjustment, or perhaps a maintenance of a more nearly stable level of personality functioning. It seems clear, however, that estrogen administration affords at least a postponement of decline in some areas of functioning. 5 references. (Author abstract modified)

078509 Bohdanecky, Z. Psychofyziologicka laborator Psychologickeho ustavu CSAV, Prague,

Czechoslovakia /The relation of psychopharmacological drugs to learning and memory./ Psychofarmaka ve vztahu k uceni a pameti. *Ceskoslovenska Psychologie (Praha).* 14(2):230-235, 1970.

The recent results in the field of psychopharamacology of learning and memory are reviewed. The effects of the representative drugs amphetamine, chlorpromazine, reserpine, anticholinergic drugs, and cholinesterase inhibitors are mentioned and their relations to neurotransmitters in adrenergic and cholinergic systems ar followed. Some corresponding neurochemical studies supporting the idea of the importance of acetylcholine and acetylcholinesterase in the problems of learning and memory are described. 21 references. (Journal abstract)

078730 Litinschi, Gh.; Fehervary, E.; Ciumageanu, D. Spitalul de Neuropsihiatrie Infantila din Paclisa-Hunoara, Rumania /Results obtained with propericiazin (8 909 R.P.) in the treatment of behavior and character disturbances in children and adolescents./ Unele rezultate privind utilizarea propericiazinei (8 909 R.P.) in tratamentul tulburarilor de comportament si caracter la copii si adolescenti. *Neurologia, Psihiatria, Neurochirurgia (Bucuresti).* 15(6):493-504, 1970.

Results obtained with propericiazin in treating behavioral and character disorders in children and adolescents are discussed. Starting from the data in literature concerning the use of propericiazin, it is proposed that a followup should be made of the effect of the drug in 45 children and adolescents admitted with behavior and character disturbances. After discussing the dosage, duration of the treatment, associations and tolerance to the drug, the results are discussed. Good and very good results were obtained in 71.1% of the cases. The results differed from case to case and were influenced by the patient's age, intellectual level, etiopathogeny and dominant symptomatology. Attention is drawn to the fact that propericiazin is a symptomatic neuroleptic that does not affect the basic nucleus of the disease and therefore should be considered as a tactical element in the therapeutical strategy of behavioral disturbances, included in an ensemble of psychologic and sociotherapeutical measures. Worthy of note were the good results also obtained in epileptic children and adolescents with behavioral disturbances. (Journal abstract modified)

078786 Gupta, B. S. Psychology Department, Government College, Kurukshetra, India The effect of extraversion and stimulant and depressant drugs on verbal conditioning. *Acta Psychologica (Amsterdam)* 34(4):505-510, 1970.

The effect of extraversion, and dexedrine and phenobarbitone on verbal conditioning is examined. A group of graduate and postgraduate students served as subjects. All the subjects were randomly assigned to 3 treatments (stimulant, depressant and placebo) and 3 extraversion groups (high, average and low). A 3 x 3 factorial design was replicated 10 times. The technique of sentence completion was used. The study supports the following conclusions: 1) introverted subjects are more conditioned than extraverted subjects; 2) dexedrine facilitates and phenobarbitone retards the conditioning process; 3) dexedrine does not improve the conditioning level of introverted subjects; 4) variability tends to increase under the influences of drugs. 25 references. (Author abstract)

078933 Goodwin, Donald W.; Freemon, Frank; Ianzito, Benjamin M.; Othmer, Ekkehard. Department of Psychiatry, Washington University School of Medicine, 4940 Audubon Avenue, St. Louis, Missouri 63110 Alcohol and narcolepsy. *British Journal of Psychiatry (London).* 117(541):705-706, 1970.

The effects of alcohol in narcolepsy are investigated in an individual with symptoms of narcolepsy whose sleep was monitored polygraphically before and after the administration of alcohol. It was found that a moderate amount of alcohol produced a coma like state in the 24 year old male patient. This response differed from a typical narcoleptic sleep attack. The patient could not be fully awakened for a several hour period and electrophysiological data obtained during the episode were uncharacteristic of narcolepsy, showing slow wave sleep and absence of rapid eye movements. It is unknown whether this represents a common response of narcoleptics to alcohol. 4 references. (Author abstract modified)

079960 Harrer, G.; Harrer, H. Landesnervenklinik, Ignaz-Harrer-Strasse 79, A-5020 Salzburg, Austria /Investigations for objectifying tranquilizer effects./ Untersuchungen zur Objektivierung von Tranquilizer-Effekten. *Arzneimittel-Forschung (Aulendorf).* 29(7):921-923, 1970.

In single experiments, it has been demonstrated that tranquilizers alleviate or suppress the vegeta-

tive effects caused by emotional stress. Yet it has not been possible to arrange an experimental setup which would allow confirmation of these findings on a sufficiently large scale for a statistical verification of the dose effect relation or of tranquilizer effects with small or medium dosage. The difficulties arising in such attempts are discussed with regard to observations made during experiments on noise - stress and the 'Lee effect.'(author abstract)

079964 Pohlmeier, H.; Schon, I.; Matussek, N. Universitat Ulm, 8871 Schloss Reisensburg, Germany /Effect of a decarboxylase-inhibitor (RO 4-4602), combined with L-dopa, on inhibited depressive patients: II. Experimental-psychological studies./ Die Wirkung eines Decarboxylase-Hemmstoffs (Ro 4-4602) und L-Dopa auf gehemmte Depressionen: II. Experimentalpsychologische Untersuchungen. *Arzneimittel-Forschung (Aulendorf).* 20(7):932-933, 1970.

A psychological study is reported of the effects of a combined medication with L-Dopa and the decarboxylase-inhibitor Ro 4-4602 or of placebo on inhibited depressive patients. The tests used were: maze test, picture recognition test, figure reconstruction test (FRT), Necker cubes, tapping, and reaction time. Positive correlations were found between the differences of the results of tapping and FRT on the one hand, and scores of a self-rating scale on the other hand, with all improved patients of the medication group and the placebo group included. These results indicate the existence of a relationship between drive state and depression. 8 references. (author abstract)

079995 Tolle, R.; Crome, A. Universitats-Nervenklinik, Osianderstrasse 22, 74 Tubingen, Germany /On activation of dreams by thymoleptics./ Zur frage der Traumaktivierung durch Thymoleptica. *Arzneimittel-Forschung (Aulendorf).* 20(7):886-887, 1970.

Our study has given no evidence that dream activity was increased by the tricyclic antidepressive substances amitriptyline, protriptyline, imipramine, chlorimipramine, and trimeprimine. Only 1 in 52 patients (1.9percent, 8.3percent of the subgroup of 12 who had never been treated by antidepressive substances before) dreamed more often than before. Our findings are consistent with the results of neurophysiological studies on imipramine that did not disclose an increase of the frequency of dreams, but in some cases even a decrease. 26 references. (author abstract)

080095 Huessy, Hans R.; Wright, Alice L. Department of Psychiatry, University of Vermont College of Medicine, Burlington, Vermont The use of imipramine in children's behavior disorders. *Acta Paedopsychiatrica (Basel).* 37(7-8):194-199, 1970.

A clinical study of the use of imipramine in the treatment of 52 hyperkinetic children is discussed. Sixty seven percent showed marked improvement on an average dose of 50mg a day. Imipramine is often used as the first drug since it often can be given on a one time a day dosage. Twenty children were followed with extensive laboratory studies which revealed no bad effects. Side effects were minimal and occurred mostly in those children who received no beneficial effects. 32 references. (Author abstract modified)

080178 Money, John. Johns Hopkins Hospital, Baltimore, Md. 21205 Use of an androgen-depleting hormone in the treatment of male sex offenders. *Journal of Sex Research.* 6(3):165-172, 1970.

The use of medroxyprogesterone acetate offers some promise, where none formerly existed, in the treatment of sex offender disorders. The drug results in a temporary functional castration and may affect brain cells that directly govern sexual and erotic functioning. While under the influence of the drug, the patient may undergo a psychic realignment in which forbidden components of sexual behavior become unforbidden and vice versa. The beneficial results of the drug may well be greatest when the onset of treatment coincides with a life crisis, arising from sexual behavior, for which there is no acceptable alternative resolution. 9 references.

081043 Lehmann, H. E.; Ban, T. A. Douglas Hospital, Verdun, Quebec, Canada Psychometric tests in evaluation of brain pathology, response to drugs. *Geriatrics.* 25(4):142, 144, 146-147, 1970.

Geriatric patients with and without psychiatric pathology and young healthy controls (total 58 subjects), exposed to experimental 'loading' with a placebo, a CNS stimulant, a CNS depressant, and a cerebral vasodilator, were given a battery of psychometric behavioral tests immediately before and without 15 minutes of each drug 'loading'. It was found that certain psychophysical and psychometric tests have diagnostic validity for the degree of organic brain and behavioral pathology in psychiatric patients. Patients with organic brain damage responded to most pharmacological agents, including placebo, with greater improvement and less deterioration of per-

formance than young healthy controls. The organic lesion patient's response is less favorable after barbiturate-like drugs and most favorable after a cerebral vasodilator. Cerebral vasodilatation is likely to be an important therapeutic factor in the treatment of psychiatric disorders, while long term use of minor tranquilizers is contraindicated.

081104 Braham, J. Department of Neurology, Tel-Hashomer Government Hospital, Israel Adjuvants to L-dopa for parkinsonism. *British Medical Journal (London).* No. 5708:540, 1970.

In a letter to the editor, a report is made of 5 Parkinsonian patients who were maintained on 1 to 2g of L-dopa for a week and their status recorded with regard to akinesia, rigidity, and tremor. Auxiliary drugs were given to the patients to determine which drugs enhance the effectiveness of relatively small amounts of L-dopa. Isoniazid (5mg/kg) daily was added and the patients were observed for a 10 day period. No change in clinical signs was noted. Another trial involved an attempt to inhibit the enzyme dopamine beta-oxidase by administration of disulfiram (Antabuse). No improvement was observed in 4 Parkinsonian patients stablized on 1g L-dopa daily and given antabuse (0.5g t.i.d.)for 9 days together with ascorbic acid. Suggestions are made for possible methods in increasing dopamine stores so that smaller doses of L-dopa can be administered to these patients thereby eliminating some of the undesirable side-effects. 5 references.

15 TOXICOLOGY AND SIDE EFFECTS

075909 Hoffer, A. author address not given L Dopa: a hallucinogen. *Schizophrenia.* 2(1):37, 1970.

This brief technical note questions the nature and effects of dopachrome in human subjects. Studies have shown that up to 10% of patients given precursor of dopachrome, will develop psychiatric symptoms. Patients with true Parkinson's disease have suffered from auditory and visual hallucinations and depression while taking L-Dopa. When used to ameliorate symptoms of parkinsonism produced by tranquilizers, L-Dopa has caused patients to become more psychotic. Therefore, it is evident that L-Dopa can be termed a psychoactive drug, much like methionine but perhaps more closely allied to the sympathomimetic amines. It is suggested that excessive quantities of dopachrome may produce schizophrenic sysmptoms much as does adrenochrome; therefore, it may be one of the schizophrenic toxins.

075980 Chrisstoffels, J.; Thiel, J. H. Psychiatric Department, University of Amsterdam, Amsterdam, Netherlands Delirium Acutum, a potentially fatal condition in the psychiatric hospital. *Psychiatria, Neurologia, Neurochirurgia (Amsterdam).* 73(3):177-187, 1970.

Delirium acutum (DA) is regarded in this study as a failure in endocrine autonomic homeostatic mechanisms. Of great importance is the early diagnosis, because the course can be particularly fulminating and a few hours may be crucial in determining the outcome. Four case histories of patients with DA and the treatment, initially with adrenocorticotropin later with corticosteroids are discussed. In 1 case serious defects remained after treatment. At present a number of factors impede an early diagnosis of imminent DA, but it is expected that the determination of the blood cortisol concentration will prove a valuable contribution to the diagnosis. Finally, it was considered whether haloperidol could have been an etiological factor in 2 cases. 12 references. (Author abstract modified)

076364 Zelman, Samuel; Guillan, Ramon. Veterans Administration Hospital, 2200 Gage Boulevard, Topeka, Kansas 66622 Heat stroke in phenothiazine-treated patients: a report of three fatalities. *American Journal of Psychiatry.* 126(12):129-132, 1970.

During a heat wave, 3 fatal cases of heat stroke were encountered. All the patients had been treated with phenothiazines, which affect temperature regulation and suppress sweating, and two with antiParkinsonian agents, which also suppress sweating. The need for lower phenothiazine dosages where possible, limited use of supplemental anticholinergic agents, and awareness of the susceptibility of phenothiazine treated patients to the hazards of extreme temperatures is stressed. 4 references. (Author abstract modified)

079254 Bejerot, Nils. Swedish National Medical Research Board, Karolinska Institutet, Stockholm, Sweden Addiction and society. Springfield, Illinois, Charles C Thomas, 1970. 299 p.

Addiction, which is a subject that cuts across at least a dozen branches of science, from chemistry and pharmacology to sociology and law, is

discussed with emphasis on psychiatry and social medicine. The aim of this book is to collect important basic facts from the various fields of science and to outline the stratification of the problem. Some new practical and theoretical proposals are presented, as well as a detailed study of the most important tendencies in the international and Swedish addiction debate. An attempt has been made to sketch a differentiated psychiatric and sociomedical plan of treatment for those suffering most severely from drug addiction and to draw up a general program for prevention. Three main points in the treatment program conclude the book: 1) strict narcotic legislation; 2) high infectivity; 3) and various therapeutic possibilities. 153 references.

079255 Bejerot, Nils. Swedish National Medical Research Board, Karolinsk Institutet, Stockholm, Sweden Concepts, definitions, terminology. *In: Bejerot, N., Addiction and society.* Springfield, Illinois, Charles C Thomas, 1970. 299 p. (p. 3-25).

The rapid change in concepts, definitions, and terminology in the field of drug addiction, and the confusion of ideas which evolved are discussed. Even if it is a little complicated to follow developments in terminology, it is unavoidable; otherwise it is likely that earlier literature on the subject may be misunderstood. In addition, the old terminology is still used, and it does describe realities which still exist. The old key term narcotics is derived from the Greek word narke, which means sleep, insensibility, and the stem of the word is also in narcosis. The term narcomania has its roots in oriental opium smoking; the trance and deep sleep which terminate this intoxication.

079256 Bejerot, Nils. Swedish National Medical Research Board, Karolinska Institutet, Stockholm, Sweden Addicting drugs. *In: Bejerot, N., Addiction and society.* Springfield, Illinois, Charles C Thomas, 1970. 299 p. (p. 26-82).

Some basic information of the most important substances causing toxicomania is presented. Data on the background, incidence, pharmacological effects, and medical use are given. The side-effects which occur when they are abused and the syndromes they give rise to are indicated. It is also necessary to know something about the legal status of the various substances and their role in the illicit drug trade. The drug industry has put on the market a number of synthetic pharmaceutical drugs which have proved to be addicting. Some of these were produced in an eeffort to find strong analgesic drugs less liable to cause addiction than morphine, but many of these substances have proved to be more dangerous than morphine itself. The addiction established by the natural central stimulant cocaine is essentially the same disease as addiction based on synthetic central stimulants. Every synthetic drug has to some extent its own special qualities - just as cocaine has - but in all essentials they seem to belong together in the same way as morphine and morphine substitutes.

079257 Bejerot, Nils. Swedish National Medical Research Board, Karolinski Institutet, Stockholm, Sweden Social-medical classification of toxicomanias. *In: Bejerot, N., Addiction and society.* Springfield, Illinois, Charles C Thomas, 1970. 299 p. (p. 83-102).

Current classifications of toxicomanias are discussed from a viewpoint of social and clinical epidemiology. It is noted that the categories are based almost exclusively on the pharmacological grouping of the substance or set of substances which cause the addictions: morphine, cocaine, or amphetamine addiction. With regard to etiology, the risk of contagion, and prognosis, it is absolutely essential to introduce a cross sectional, social - medical dimension across the pharmacological groups, a classification based on the generating factors. In social medicine, classifications of this type are called epidemiologic, and the term is used here in a wider sense than in connection with infectious diseases.

079914 Gaind, Raghunandan; Saran, Brij Mohan. Guy's and St. Olave's Hospitals, London, S.E. 16, England Acute lithium poisoning. *Postgraduate Medical Journal (London).* 46(540):629-631, 1970.

A woman aged 45 years old with severe depression, while receiving prophylactic treatment with lithium carbonate, (250mg 3 times daily), surreptitiously took a single large overdose of lithium carbonate and suffered acute lithium poisoning with resultant loss of consciousness, and ataxia, leading to epileptiform fits. Treatment with 0.16 molar lactate i.v. was successful. Severe intoxication from lithium salts may also occur as a result of cumulative overdose in a patient on lithium treatment, or because of decreased excretion of lithium in a patient receiving optimal subtoxic therapeutic dosage. At present the treatment of acute lithium poisoning is primarily symptomatic and supportive. 20 references.

079915 Singer, K.; Wong, M. Hong Kong Psychiatric Centre, High Street, Hong Kong Severe persistent chorea with phenothiazine therapy: report of a case. ***Postgraduate Medical Journal (London).*** **46(540):633-634, 1970.**

A paranoid schizophrenic Chinese man aged 37 years old, was treated since age 19 years old with phenothiazines. At the age of 31 years old he had a tremor affecting the tongue, lips, shoulders and hands, and the movements gradually became more severe and choreiform, spreading from the face to the neck, limbs and trunk, resulting in substantial impairment of manual dexterity, locomotion and speech. His condition remained unchanged 10 months after withdrawal of phenothiazines. Family history was negative for chorea or other neurological illness. Dyskinesia following protracted administration of phenothiazines should be considered in the differential diagnosis of chorea of unknown origin. 9 references.

079950 Hippius, H.; Logemann, G. Psychiatrische Klinik II der Freien Universitat Berlin, Nussbaumallee 36, 1 Berlin 19, Germany /On the effect of dioxyphenylalanine (L-DOPA) on extrapyramidal hyperkinesia due to neuroleptic long-term medication./ Zur Wirkung von Dioxyphenylalanin (L-DOPA) auf extrapyramidalmotorische Hyperkinesen nach langfristiger neuroleptischer Therapie. ***Arzneimittel-Forschung (Aulendorf).*** **20(7):894-896, 1970.**

In 40 cases of hyperkinesia due to neuroleptic long-term medication, single doses of L-DOPA were applied (100mg; slow i.v. injection). In 12 out of 40 patients, the hyperkinetic symptoms were enhanced. The enhancement of hyperkinetic phenomena by L-DOPA is connected with an effect on mood and drive on the one hand and with a reduction of hyperkinetic (Parkinson-like) symptoms on the other. It can be assumed that these interrelated effects of L-DOPA express the responsiveness of the extrapyramidal system. 11 references. (author abstract)

079990 Bauer, A. Neurologisch-Psychiatrischen Klinik des Stadtischen Krankenhauses, Gotenstrasse 6-9, 632 Frankfurt/M.-Hochst, Germany /Drug controlled addiction./ Die medikamentos gesteuerte Sucht. ***Arzneimittel-Forschung (Aulendorf).*** **20(7):875-876, 1970.**

Outpatient treatment with chlormethiazol cannot be recommended. Potential addicts who show signs of marked instability, depravation and social decline and who are discharged from the hospital after a short withdrawal period to continue treatment with chlormethiazol on an outpatient status, will use this drug as a substitute. For the 'secondary addicts', however, who are not instable but who suffer from neurotic syndromes or from psychic tension as a consequence of permanent environmental conflict, chlormethiazol is more likely to prevent a development towards drug habituation and successive dose increase than are the well known tranquilizers which have the disadvantage of additional hypnotic medication being often required; patients also frequently combine them with alcohol. Chlormethiazol, on the other hand, can be gradually reduced or, because of its minimal toxicity, retained for long-term medication, if necessary. 18 references. (author abstract modified)

079991 Peters, U. H.; Seidel, M. Neuro-Psychiatrischen Klinik der Johannes-Gutenberg-Universitat, Langenbeckstrasse 1, 65 Mainz, Germany /Abuse of and addiction to diazepam./ Medikamentenmissbrauch und Sucht bei diazepam. ***Arzneimittel-Forschung (Aulendorf).*** **20(7):876-877, 1970.**

In 3 cases of exclusive diazepam (Valium) addiction, the drug had been taken in daily doses of 80 to 120 mg for several years. According to these observations, the tranquilizing effect of the drug seems to decrease with continued use, whereas the muscle relaxing effect is still enhanced with the resulting dose increase. Withdrawal caused a transient withdrawal syndrome with tremor and agitation, anxiety, feelings of weakness, and in some cases delirious manifestation. Diazepam abuse, however, is considerably more frequent in alcoholics after withdrawal, or as a hypnotic. But in these cases, the daily dose hardly ever exceeds 30mg. Continued use can provoke depressive manifestations which may give rise to diagnostic errors. As diazepam is a drug applied in many different fields of medicine its use is difficult to control. The risks are not yet sufficiently known. 3 references. (author abstract)

079992 Liebaldt, G. P. Neuropathologisches Laboratorium der Universitatsnervenklinik, Fuchsleinstrasse 15, 87 Wurzburg, Germany /The problem of cerebral edema during combined psychotropic drug therapy./ Zur frage des hirnodems bei kombinierter psychopharmakologischer Therapie. ***Arzneimittel-Forschung (Aulendorf).*** **20(7):879-882, 1970.**

The question of toxicological etiology is raised by the example of a case of cerebral edema during combined psychotropic medication. Considering our present knowledge of influences on the bloodbrain barrier, it appears necessary to take into account the elimination characteristics of the single and of the differently combined psychotropic substances. As only the undissociated part of a substance can permeate the bloodbrain barrier, 'pKA' value has a special clinical therapeutic importance. In addition, the 'biological halflife' and the 'lipoid solubility' of the drugs used should be taken into consideration for estimating the risks of a combined medication. Thesole orientation of psychotropic drug therapy towards 'target symptoms' must be questioned in such cases. 21 references. (author abstract)

079996 Hippius, H.; Lange, J. Psychiatrische Klinik II der Freien Universitat Berlin, Nussbaumallee 36, 1 Berlin 19, Germany /On problems of late extrapyramidal hyperkinesis due to neuroleptic long-term therapy./ Zur problematik der spaten extrapyramidalen Hyperkinesen nach langfristiger neuroleptischer Therapie. *Arzneimittel-Forschung (Aulendorf).* 20(7):888-890, 1970.

The manifestation rate of extrapyramidal hyperkinesia has been studied in an unselected group of 668 hospitalized psychiatric patients. A comparison of manifestation rates in patients who had never received neuroleptic medication and in patients with neuroleptic long-term therapy revealed a significantly higher rate of hyperkinetic manifestations in the patient group receiving neuroleptic medication. By breaking down the findings according to age and sex of patients and according to intensity of neuroleptic treatment, and by comparing manifestation rates of outpatients and of hospitalized patients, we have obtained results indicating that extrapyramidal - hyperkinetic manifestations depend not only on the neuroleptic therapy, but also on the patients' individual dispositions. 14 references. (author abstract)

080110 no author. author address not given Diethylpropion psychosis. *Medical Journal of Australia (Sydney).* 2(23):1052-1053, 1970.

Case histories relating psychosis with the use of the appetite suppressant are reviewed in this comment on diethylpropion psychosis.It is believed, in spite of the few reports of adverse psychiatric reactions to the use of the drug, that abuse and addiction in susceptible individuals might have been predicted from knowledge of the stimulating and sympathomimetic properties and the relationship to amphetamine of diethylpropion. A warning is believed to be justified in the light of experience, of the possible dangers of diethylpropion when the drug is given to patients showing features of major personality disorders who have abused amphetamine or related compounds in the past. It is inferred that previous ingestion of amphetamine or related substances is one of the factors conducive to a psychotic illness when diethylpropion is taken in excessive amounts. 6 references.

081082 Herson, R. N. Grays, Essex, England Mental symptoms in parkinsonian patients treated with L-dopa. *Lancet (London).* No. 7675:721, 1970.

In a letter to the editor, a case is reported of a 73 year old man suffering from arteriosclerotic Parkinsonism and dementia who was treated with amantadine hydrochloride. On a dose of 100mg daily, he became more assertive and interested in his surroundings, but when the dose was doubled he deteriorated rapidly, becoming drowsy, uncooperative and unresponsive. He was admitted to a hospital where he died of bronchopneumonia. It is recommended that both L-dopa and amantadine be used with caution in similar cases.

081090 Sacks, Oliver W.; Kohl, M. Beth Abraham Hospital, Bronx, New York 10467 Incontinent nostalgia induced by L-dopa. *Lancet (London).* No. 7661:1394, 1970.

In a letter to the editor, it is noted that one of the effects of L-dopa, when given to certain postencephalic patients, is to reactivate symptoms and behavior patterns present at a much earlier stage of the disease and long dormant. Such lost symptoms may include respiratory crises, oculogyric crises, iterative hyperkinesis, tics, myoclonus, bulimia, polydipsia, satyriasis, central pain, forced affects, memories, dreams, thought systems, and moral postures. A case is presented of a 63 year old woman who had had progressive postencephalic parkinsonism since the age of 18 and had been institutionalized in a state of continuous oculoguric trance for 24 years. L-dopa produced a dramatic remission of symptoms with nearly restored speech and movement, followed by psychomotor excitement with increased libido. This period was marked by nostalgia, identification with the patient's youth, and an upsurge of remote sexual memories and allusions. It is suggested that each individual possesses an almost

infinite supply of memory traces which can be reactivated under conditions of extreme excitement; it is regarded as unlikely that the patient's memories had been 'repressed' in the psychoanalytic sense. Forced reminiscence can be induced by cortical probes, migraine, epilepsy, and other crises as well as by L-dopa. 3 references.

081135 Niedermeyer, E.; Blumer, D.; Holscher, E.; Walker, B. A. The Johns Hopkins Hospital, 601 North Broadway, Baltimore, Maryland 21205 Classical hysterical seizures facilitated by anticonvulsant toxicity. *Psychiatric Clinica (Basel).* 3:71-84, 1970.

In 3 patients, unequivocal hysterical seizures with classical posturing ('arc de cercle') were observed. Two of these patients had a history of mild epilepsy and were therefore placed on anticonvulsive therapy; the third patient, an achondroplastic dwarf, was treated with anticonvulsants since her hysterical manifestations were initially considered epileptic. In all patients, the hysterical seizure frequency increased under anticonvulsive therapy and reached enormous proportions with further increases of medication. The electroencephalogram showed excessive diffuse slow activity due to cerebral toxicity and, in 2 cases, there was also neurological evidence of a toxic brain disturbance. This toxic response was obviously caused by Mysoline (primidone) in 2 cases and by Dilantin (diphenylhydantoin) in the third patient. Gradual increase of the anticonvulsive medication was followed by attenuation and eventual disappearance of hysterical seizure manifestations. Classical hysterical seizures have become rare in the course of this century. In the reported cases, both organic and psychodynamic - psychosocial predisposing factors were presumably present whereas the drug induced cerebral toxicity was considered a facilitating factor. 11 references. (author abstract)

081150 Celesia, Gastone G.; Barr, Arlene N. Department of Neurology, University of Wisconsin Medical School, Madison, Wisconsin 53706 Psychosis and other psychiatric manifestations of levodopa therapy. *Archives of Neurology.* 23(3):193-200, 1970.

Levodopa is an effective drug for the treatment of parkinsonism. However, mental disturbances occur not infrequently during its administration. Sixteen of 45 patients receiving levodopa developed psychiatric phenomena. Psychosis, acute anxiety, euphoria, and other psychic phenomena are described in detail. Fourteen of the 16 patients, or 87.5%, had associated buccolingual or generalized dyskinesia. This association of psychic disorder with buccolingual or generalized dyskinesia is characteristic of levodopa toxicity. The levodopa psychosis - dyskinesia complex is reversible and most frequently controlled by dimunition of levodopa dose. It occurs mostly in patients with associated organic brain syndrome or those suffering from postencephalitic parkinsonism. The interesting relationship between psychiatric manifestation, dyskinesia, basal ganglia, and biogenic amines is discussed. 25 references. (author abstract)

16 METHODS DEVELOPMENT

077404 Ahmad, R.; Gillingham, F. J.; Hanieh, A.; Pullar, I. A.; Weddell, J.; Ashcroft, G. Department of Surgical Neurology, The Royal Infirmary, Edinburgh, Scotland Akinesis following stereotactic surgery for parkinsonism - the use of L-dopa. *Confinia Neurologica (Basel).* 32(2-5):128-134, 1970.

The finding in 1960 that Parkinsonian patients have lower levels of dopamine in the basal ganglia and substantia nigra has led to better treatment with oral or intravenous dihydroxyphenylalanine (dopa). Twenty eight patients were treated postoperatively with 4 to 6g daily of L-dopa with marked improvement noted especially in bradykinesis, gait and speech; tremor generally remained unchanged. Nausea and vomiting were seen to be the most troublesome side-effects. Ten of seventeen operated patients and 9 of 11 unoperated subjects showed noteworthy improvement, with no difference in effect of the dopa on patients with thalamic lesions as opposed to pallidal lesions. The drug appears to be tolerated best if begun at a low dosage and slowly increased over a 2 week period to a maximum of 8g daily. Any side -effects can be reversed by reducing the dosage of the drug. 13 references.

080040 Moldenhauer, B. 19 Karmeliteweg, 1 Berlin 28, Germany /Clinical and ambulant testing with fluphenazine decanoate Lyogen-Depot in the long term treatment of psychiatric disease./ Klinische und ambulante Erfahrungen mit dem Fluphenazin-Decanoat Lyogen-Depot bei der Dauerbehandlung psychiatrischer Krankheitsbilder. *Medizinische Welt (Stuttgart).* 70(25):1150-1154, 1970.

The efficacy of fluphenazine enanthate and of fluphenazine decanoate in the treatment of psychotic patients is discussed. Testing with oral and depot treatment (Fluphenazine Decanoate Lyogen-Depot) was carried out in order to evaluate the areas of effective treatment. The depot treatment was found more effective than the Fluphenazine Enanthate having fewer side-effects upon circulation and extrapyramidal systems. The depot neuroleptic treatment, both in hospitalized and ambulant patients over a long period has proven more effective in prolonging the remission stability of the schizophrenic patient, and is a surer way of administering the medication than is the oral method. As for all long-term therapy, the patient must be kept under observation at all times. The therapy is also highly recommended for the criminally insane type of patient. A total of 428 patients received the depot treatment. 18 references.

075843 Rickels, Karl; Howard, Kay. 203, Piersol Building, University Hospital, 3400 Spruce Street, Philadelphia, Pennsylvania 19104 The physician questionnaire: a useful tool in psychiatric drug research. ***Psychophamacologia (Berlin).*** **17:338-344, 1970.**

A 10 item physician questionnaire, a simple instrument for rating neurotic symptomatology, is discussed. The data were factor analyzed according to the principal components method with varimax rotation using a computer program developed by Clyde et al. Analyses of covariance were performed to test for treatment (medication) differences in 3 selected studies using both the standard cluster, and the newly derived factor scores. The results of a factor analysis were presented. The sensitivity of both the 3 derived factor and 2 clinical cluster scores in detecting differences among psychotropic drugs was demonstrated. 9 references. (Author abstract modified)

076327 Cole, Jonathan O. Boston State Hospital, Boston, Massachusetts Psychopharmacology: the picture is not entirely rosy. ***American Journal of Psychiatry.*** **127(2):224-225, 1970.**

Drug therapy has helped American psychiatry a great deal, but there is much to be desired for the future. The antipsychotic, antidepressant, and antianxiety drugs, although reasonably useful, are often not effective enough. There are not useful drug therapies for amphetamine dependence and chronic alcoholism, and little is being done to help in mental retardation and geriatrics. The complex and expensive requirements that have been placed on commercial drug development by well meaning regulatory agencies has slowed new research and development.

076346 Finnerty, Frank A., Jr. Georgetown University Medical Center, Washington, D. C. Treatment of labile hypertension. ***Psychosomatics.*** **11:339-341, 1970.**

It is useful to classify hypertensive subjects into groups having predominantly supratentorial, arteriosclerotic, or vasospastic disease. Patients with supratentorial disease suffer from headaches, dizziness, excessive perspiration, tachycardia, and fatigue. Although the diastolic and systolic arterial pressures are high, there is no evidence of vascular disease, the heart is not enlarged, and all laboratory tests produce normal results. The primary aim of therapy in these patients should be the relief of anxiety. Amytal sodium or reserpine show good results. Reserpine relieves anxiety and tension and lowers the blood pressure; it is not habit forming. It has toxic reactions, however, ranging from weight gain and gastric acidity to severe mental depression. It should not be prescribed for patients who are obese or who have a history of peptic ulcer or mental disease. The patient is also put on a reducing diet if he is overweight. 1 reference.

076351 McClellan, Thomas A.; Cowan, Gary. Veterans Administration Mental Hygiene Clinic, Fort Snelling, St. Paul, Minnesota 55111 Use of antipsychotic and antidepressant drugs by chronically ill patients. ***American Journal of Psychiatry.*** **126(12):1771-1773, 1970.**

Of the patients in a Veterans Aministration mental hygiene clinic, 81% receiving antipsychotic and antidepressant drugs were studied as to their use of medication and the extent to which they accurately reported their use. It was found that a small number were not taking any of the medication, that a substantial number were taking amounts significantly less than that prescribed, and that these patients were not volunteering this information to their therapist. 1 reference. (Journal abstract)

076508 Garber, Robert S. Carrier Clinic, Belle Mead, New Jersey The impact of psychopharmacology on medicine and psychiatry. ***Psychosomatics.*** **11(5):386-390, 1970.**

The development of psychopharmacology is traced from about 3,000 years ago, when Assyrians began using hashish to barbiturates and bromides and on to the modern era which began less than 20 years ago. Chemotherapy is dated from 1952 when chlorpromazine was introduced in France. By 1969, the National Clearinghouse for Mental Health Information had published a compendium which lists about 852 compounds of which very few were in use 20 years ago. A few drugs mentioned are: imipramine, amitriplyline, resperine, thioxanthene, fluphenazine, penothiazines, trifluperidol, thorazine, and iproniazid. Attempts have been made in the past 2 years to take stock of this impressive and rapidly growing psychopharmacopeia. 20 references.

078106 No author. Author address not given Lithane: the story of lithium carbonate. *Occupational Health Nursing.* 18(5):25-27, 1970.

Lithane, lithium carbonate, is approved by the United States Food and Drug Administration for treating the manic phase of manic-depressive psychosis. Research has found it to be a potent antimanic agent, 70 to 80% effective within 5 to 10 days in a manic patient. However, when administering this compound it is extremely important to have adequate kidney function and absence of salt-free diet to prevent lithium from rising to toxic levels. In 1949, Dr. John J. F. Cade, an Australian psychiatrist, published the first of his papers on the use of lithium in the treatment of mental patients. Dr. Ronald Fieve, Chief of Psychiatric Research at New York State Psychiatric Institute and Associate Professor of Psychiatry at Columbia University, began using lithium in 1958, and treated several hundred cases of manic-depressive illness. Lithium is not effective against the depressive stage of the disease. Dr. Fieve believes lithium will largely replace electroshock within the next decade. Progress of the drug has been controversial, possibly since it cannot be patented. However, Pfizer's J. B. Roerig Division completed an extensive laboratory toxicology program supported by clinical investigations, and has produced over 1 million tablets for use by investigators. The company also collected and submitted to the FDA, voluminous research data in connection with a new drug application.

078422 Blinder, Martin G. Family Therapy Institute, San Francisco, California Lithium carbonate in therapy. *Current Psychiatric Therapies.* 10:100-104, 1970.

The use of lithium carbonate in therapy of recurrent hypomania, recurrent depression, psychotic excitement, premenstrual tension and anxiety is discussed. Lithium ion is believed to be almost unique as a psychiatric drug: when used knowledgeably, it is effective in perhaps 3 or 4 cases, its effects are specific and predictable, it produces virtually no side effects after the first week of administration, and it never causes a 'medication feeling.'Administration and toxicity of lithium (usually the carbonate) are discussed. 5 references.

078429 Kaim, S. C. Staff for Alcoholism and Related Disorders, Veterans Administration, Washington, D. C. Optimal therapy of the alcohol withdrawal state. *Current Psychiatric Therapies.* 10:154-160, 1970.

In research conducted in alcoholism, it is essential to define the alcoholic state and specify the signs and symptoms peculiar to the state under investigation, as well as stipulate criteria for including the patients in the study. Otherwise, the studies may have little meaning. Research on the alcohol withdrawal state is reviewed in the introduction to a discussion of optimal therapy of the alcohol withdrawal state. Studies with the most rigorous research design indicate that the syndromes are most effectively treated with drugs that are adequate pharmacologic substitutes for alcohol. Clinical aspects of alcohol withdrawal are discussed and some therapeutic methods are reviewed. A suggested regimen is presented including chlordiazepoxide therapy and treatment for dehydration and electrolyte imbalance and nutritional deficiencies. Special consideration is given to management of delirium tremens. The treatment regimen for the latter differs in adding treatment for circulatory collapse or shock and for hyperthermia. Chlordiazepoxide is the preferred drug, with paraldehyde as alternate. Hospitalization is required for all but the mildest alcohol withdrawal syndromes. 13 references.

079144 Freeman, Roger D. Department of Psychiatry, University of British Columbia, Vancouver 8, British Columbia, Canada Review of medicine in special education: another look at drugs and behavior. *Journal of Special Education.* 4(3):377-384, 1970.

A review of literature on the use of drugs in the treatment of behavior and learning disorders in children is presented. Classification by commonly utilized target symptoms or syndromes is the basis for the discussion. The difficulties in assessing drug effects because of other factors, especially development, operating in the child are noted. The few general statements which emerge from the review are that: 1) severely disturbed behavior (thinking disorders, bizarreness, aggression, high anxiety level) should be first managed with a major tranquilizer, rather than a stimulant; 2) the distractible, hyperactive nonpsychotic child may be first given a fair trail of stimulants before employing the tranquilizers, which may depress learning or performance; 3) haloperidol is a promising method of managing presistent and multiple tics; 4) thioridazine may be useful in reducing stereotyped behavior, at least in retar-

dates. There seems to be little scientific support (beyond individual preference) for the usefulness of the antihistamine, anticonvulsant, or minor tranquilizing agents. 43 references. (Author abstract modified)

079962 Mertens, Hans Georg; Lutzenkirchen, Hans. Neurologische Universitatsklinik, Luitpoldkrankenhaus, 87 Wurzburg, Germany /Neuropsychotropic drugs in the treatment of so-called pain syndromes./ Neuropsychopharmaka in der Behandlung der sog. Schmerzkrankheiten. ***Arzneimittel-Forschung (Aulendorf).*** **20(7):928-930, 1970.**

The treatment of chronic pain syndromes must be carried out according to rules differing from those to be observed in acute pain states: different substances must be used. A pain syndrome with a tendency to become self-sustaining can be most effectively cured by the systematic application of psychotropic drugs. As a preliminary result of observations, 10 rules have been formulated. The authors hope to stimulate the discussion on the treatment of pain syndromes in order to arrive at a more scientific and exact method of their treatment, by rejection or corroboration of such empirically obtained but statistically not confirmed observations. It will be important to find out which syndromes can be influenced more by neuroleptic and which by thymoleptic medication; also, whether it is necessary to use a combined neuroleptic and thymoleptic medication in certain cases, which is difficult to explain theoretically. 15 references. (author abstract)

079987 Modestin, J. Forschung Medizin, Monbijoustrasse 115, 3000 Bern, Switzerland /Psychotropic drug therapy and the pharmaceutical industry./ Psychopharmaka-Therapie und die pharmazeutische Industrie. ***Arzneimittel-Forschung (Aulendorf).*** **20(7):877-879, 1970.**

Industrial research in the field of psychopharmacology for the development of new substances, as well as the clinical trial of every promising substance synthetized in industry, are certainly justified. The number of psychotropic drugs which are at the disposal of the physician is continually increasing. Also their general use, that is, outside the control of the specialist, is extending. This development is advanced by influences from the industry (recommendations for indication on the base of symptoms,which increases the tendency to extend the application of a drug) as well as the still limited medical knowledge (difficulties in defining 'normality' or 'illness' in psychiatry) and general influence and demands of our time. The unqualified use of psychotropic drugs can lead to abuse. Therefore, caution in the handling of these drugs is an indispensable preventive measure. 4 references. (author abstract)

080002 Seal, R. E. Department of Psychiatry, St. Vincent's Hospital, Victoria Parade, Fitzroy, Victoria, 3065, Australia The current status of the hallucinogenic drugs. ***Australian and New Zealand Journal of Psychiatry (Melbourne).*** **4(2):64-67, 1970.**

A brief review is presented of the current use of hallucinogenic drugs among lay and medical people in general, and particularly in Victoria, Australia. During the mid 1960's, LSD, psilocybin, and psilocin were used less by many psychiatrists who found it disappointing clinically and often dangerous and unpredictable in its effects on the patients' emotions and on their life adjustments. Increasing numbers of lay people were using LSD because of the attraction of its mystique and the aura of mystery and magic that surrounded its use and abuse. Current social philosophies in which traditions were challenged and better communication, which has created a new awareness in the younger generations, are believed to have contributed to this increased use of the mind expanding drugs. Legislation against the use of these drugs has produced a decrease in their use with a swing towards marijuana which is gaining recognition as being not as dangerous as was once believed. Psychiatrists have reported good results with these drugs in cases of anxiety neurosis, hysteria, mixed neurosis, character disorders, psychosexual disorders, and alcoholics and drug dependent personalities. However, none felt that these drugs provided a complete or absolute answer, and most felt that their use greatly increased rather than decreased their work load. 8 references.

080007 Imlah, N. W. All Saints' Hospital, Birmingham, England Psychiatric community care system: use of long-acting phenothiazines. ***Medical World (London).*** **108(6):14, 1970.**

Despite great developments in the psychiatric community care system at the All Saints' Hospital in Birmingham, England, the problem of the relapsing schizophrenic patient continues because of failure to maintain adequate medication. The

development of the long acting phenothiazines, and the evidence of the high efficacy of these drugs obtained from clinical trials in the hospital, has provided a means to a solution of this serious problem. The organization and integration of this therapy into the program of aftercare must be effected. At the present time, 300 schizophrenics are maintained on Modecate at All Saints' Hospital. A special clinic has been set up for drug administration; should a patient fail to keep an appointment, a nurse visits him, gives him his injection and makes another appointment. This system of therapy has been effective in keeping the patient in the community, in employment and preventing relapse.

080096 Knobel, Mauricio. University of Buenos Aires, Buenos Aires, Argentina /The use of psychopharmacology in children and adolescents./ Die Anwendung Von Psychopharmaka bei Kindern und Jugendlichen. *Acta Paedopsychiatrica (Basel).* 37(7-8):200-212, 1970.

The use of psychopharmacology in child psychiatry and factors which must be considered in pharmacological studies are discussed. The study of psychodynamic factors, particularly from a psychoanalytical point of view, may elucidate the real drug action. Ignorance of child psychopathology is at the root of the disregarding of these aspects of pedopsychiatric psychopharmacological investigation. The result has been doubt of, or contradictory reports about, drugs which have proved to be effective in this field. Four fundamental variables must be considered: the child, the mother, the family, the physician. Each of them may manifest itself in placebo attitude (in favor of the curative actions) or in an antidrug attitude (undoing the result of the medicament or provoking toxic reactions or side effects). The drug, as a concrete object introduced into the organism, has, apart from its biochemical action, a symbolic significance. 32 references. (Author abstract modified)

080097 Lesser, Leonard I. Child Guidance Center of Orange County, Costa Mesa, California The Children's Psychopharmacology Clinic: its role within a total program for children's psychiatric services. *Acta Paedopsychiatrica (Basel).* 37(7-8):212-222, 1970.

A psychopharmacology clinic for children in California is discussed. The Children's Psychopharmacology Clinic of the LAC/USC Medical Center, established within the framework of the Children's Psychiatric Out-patient Clinic to treat children with central nervous sytem damage, evolved into functions of: 1) increasing service needs of the institution, 2) aiding in rendering crisis services to children and their families, and 3) establishing a reservoir of appropriate case material for inpatient services and teaching assignments. During this study, some 300 children and their families were treated, approximately 30% of whome were psychotic. In a large number, the incorporation of psychopharmacological agents enabled the disturbed child to remain within his home while more distant goals could be planned. Preliminary studies suggest that psychopharmacological agents bring about a rapid symptomatic improvement in the child, followed by a plateau which is maintained. If this can occur at a point of crisis, intervention can prevent deterioration of the child's social milieu and facilitate the recovery process. 14 references. (Journal abstract modified)

080350 DiMascio, Alberto. Tufts University School of Medicine, Medford, Massachusetts Psychopharmacology in children: problem areas, methodological considerations, assessment techniques. *Massachusetts Journal of Mental Health.* 1(1):8-24, 1970.

The area of psychopharmacology in children is reviewed and evaluated as to problems, methodological considerations and assessment techniques. The use of psychotropic drugs in emotional and behavioral disorders of children is in a much less advanced state than the uses of these drugs for adults, less than 500 articles have been published in the former area. The number of drugs assessed, the lack of information on dosage and adverse or toxic reactions, the methods of quantitatively assessing efficacy of the drugs, and many other factors contribute to the state of affairs in psychopharmacology in children, a state termed 'sad' and believed to exist because of a number of logical clinical, ethical, theoretical, pragmatic and legal issues that produce a multiplicity of problems -- leading to the concentration of research effort on adult psychopharmacology. Experimental considerations which must be faced before advancement in child psychopharmacology may be achieved are: classification or symptomatology and diagnosis; assessment of severity of illness; the age or maturational state of the child; and other organismic

variables such as intelligence quotient levels and sex. Other considerations are: the dosage in drug therapy or drug research, as related specifically to children; and the assessment techniques and problems (including assessment of adverse drug effects), with evaluation of the drug induced changes in the children being made from as many points of reference as possible. The aims, requirements and value of 3 phases of research studies into psychopharmacology for children are outlined. The phases are: early drug trials, large scale double-blind studies and late - state studies. An outline of types of objective measures or scales is presented, also. 23 references.

080394 Vinar, O. Vyzkumny ustav psychiatricky, Prague, Czechoslovakia /Current problems of clinical psychopharmacology./ Soucasny stav klinicke psychofarmakologie. ***Ceskoslovenska Psychiatrie (Praha).*** **66(1):6-12, 1970.**

The principal characteristic of the current state of clinical psychopharmacology is the ongoing evaluation of the effects of modern psychotropic drugs. Controlled clinical experiments have brought clear evidence of the therapeutic efficacy of neuroleptic drugs in schizophrenic psychoses. In terms of the drug - placebo difference, fundamental schizophrenic symptoms (social withdrawal, thought disorders) are being relieved more than accessory symptoms (halluciations, delusions) and these in turn more than symptoms which are not typical for schizophrenia (anxiety, depression, disorientation). Neuroleptics were found to prevent the development of symptoms in schizophrenic patients more than placebos. Evidence of antidepressant effects of phenothiazines has been rendered. The mass consumption of anxiolytics is of mental hygienic concern, and its social causes and repercussions are studied by social psychopharmacology. The search for scientifically valid differential indications of commercially produced drugs is the most important task of clinical psychopharmacologists. 13 references. (journal abstract modified)

081072 Gitlow, Stanley E. Department of Medicine, Mount Sinai Medical School, New York, New York The pharmacological approach to alcoholism -- Part 2. ***Maryland State Medical Journal.*** **19(5):103-106, 1970.**

The pharmacological treatment of alcoholism is described and discussed from the viewpoint that the most important factor in the rehabilitation of an alcoholic lies in his motivation to quit drinking. The use of sedative agents (Librium, Valium, Miltown, Equanil, Doriden) is frustrating since it is merely a substitution and not a cure. Sedatives, which may be given in conjunction with chlorpromazine or promazine, should be given in the hospital where the physician has complete control of the patient and the dosage. Long-term therapy for recidivism or compulsivity is necessary after withdrawal. However, the simple act of prescribing sedatives in order to relieve anxiety symptoms guarantees failure almost 100% of the time. Antabuse, on the other hand, does not relieve anxiety symptoms but rather produces a toxic reaction when taken with alcohol. Willingness to take Antabuse represents good motivation. Antabuse stops compulsive drinking completely. By taking Antabuse daily, the patient is faced with the constant decision of whether to drink or not. He is totally responsible for his decision against alcohol and it is thus more meaningful. The long-term treatment of alcoholism must be directed towards increasing the abstinent alcoholic's capacity to tolerate anxiety without recourse to sedatives. The terms addiction, habituation, cross-addiction and withdrawal are defined.

081087 No author. Author address not given Sleeping pills. ***British Medical Journal (London).*** **No. 5718:296-297, 1970.**

A report is presented of an article by Evans and Ogunremi in the same issue in which a series of experiments is described on the effect of chloral hydrate (0.8grain), dichloralphenazone (1.3grain), and dephenhydramine on the sleep - waking cycle. The first drug effected a slight suppression of R.E.M. sleep; the latter 2 had little or no effect on R.E.M. sleep. The effect on the duration of R.E.M. sleep is not the only criterion for the effectiveness of a hypnotic drug; the drug's effect on the intensity of the R.E.M. phase must also be considered, as must the hangover the drug induces. Barbiturates, glutethimide and methaqualone reduce the intensity of R.E.M. sleep. Unacceptable hangovers have been induced by nitrazepam and amylobarbitone sodium. In view of their low potential for abuse, the benzodiazepines, and especially nitrazepam, may be regarded as the preferable drugs when hypnotics must be prescribed.

081110 Dlabac, A. Research Institute for Pharmacy and Biochemistry, Prague, Czechoslovakia The

importance of research in biogenic amines for the experimental psychopharmacology. *Activitas Nervosa Superior (Praha).* 12(3):215-225, 1970.

The present knowledge of the physiology and biochemistry of adrenergic and serotoninergic neurones in the CNS is reviewed, and new information published presumably in 1969 is summarized. The gathering of this information was brought about by technical progress in the study of intracellular processes. It is apparent that the studies of biochemical kinetics are of fundamental importance. Under physiological and pathological circumstances, the regulatory phenomena take place and the rate of biosynthesis, turnover, and inactivation of neurotransmitters is variable. Drugs, too, influence the rate of biochemical processes for the particular monoamines in the CNS and here are the possibilities of a more precise research of the mechanism of action of psychotropic drugs. 101 references. (author abstract)

081147 Pustisek, B. Orthopadische Klinik Kassel, 345 Wilhelmshohe Allee, 35 Cassel-Wilhelmshohe, Germany /Clinical results of the testing for analgesic effect of dextropropoxyphene in combination with a psychotropic preparation (Tropax)./ Klinische Ergebnisse der Prufung auf analgetische Wirkung von Dextropropoxyphen und einem Psychopharmakon. *Arzneimittel-Forschung (Aulendorf).* 20(7):932, 1970.

The postoperative or posttraumatic stages in orthopedic treatment call for an analgesic drug which can be administered for the alleviation of pain without harmful side effects. Tropax is ananalgesic combination preparation containing as its main ingredient dextropropoxyphene. The other ingredients are dimethylaminophenyldimethylpyrazolon and flupenthixol. During a 5 month period, 98 patients were tested in a double-blind experiment in which 49 were given Tropax, and the other 49 a comparable preparation. In 82% of the cases the indication for treatment was the postoperative course, the other 18% were being treated conservatively. Out of the 49 patients treated with Tropax, 18 showed improvement, 24 were unchanged, and 7 worsened; for the other 49 patients there was improvement in 9, no change in 30, exacerbation in 9, and 1 case which was not evaluated. Both medications showed good tolerance.

081392 Barbeau, Andre; Cooper, Irving S. Department of Neurobiology, Clinical Research Institute of Montreal, Montreal, Canada L-Dopa in the treatment of Parkinson's disease. *Medical Opinion and Review.* 6(8):82-87, 1970.

The administration of L-Dopa, the biosynthetic precursor of dopamine, has been a highly successful treatment of Parkinson's disease since its introduction in 1961. At low doses, L-Dopa probably corrects the symptoms of akinesia and rigidity by permitting a renewed supply of dopamine to reach dopamine sensitive receptors in the striatum. At high levels of its administration, sites outside the striatum are also involved and there may be displacement of other neurotransmitters. The excretion of dopamine in Parkinson's disease will be low only if akinesia is the predominant symptom. L-Dopa treatment, by virtue of its complex variability, has facilitated a reassessment of the neurophysiological substratum to dyskinesis and to the psychiatric manifestations of motor diseases. L-Dopa has replaced thalamic surgery for relief of parkinsonian tremor, and a trial of this therapy should be approached before surgery is considered. Its toxic effects are nausea and vomiting, which can be circumvented by slowing the increases of the dose (3 to 5g daily). Therapy should be instituted with the patient hospitalized and dosage graduated slowly. In good risk candidates for operation, it is possible to relieve tremor and rigidity at the time of operation at least 93% of the time. Surgical investigations have contributed to the widening insight into the neural mechanisms of the motor symptoms of parkinsonism. A survey indicates a general facilitation of alpha motoneurones in relation to gamma motoneurons, a result of pathologic involvement of the suprasegmental centers.